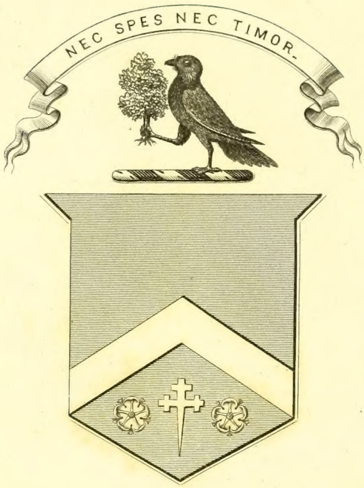

George C. Karop.

G. C. Harop.

From J. W. Nunn F.R.C.S.

Middlesex Hospital. W.

1874.

THE NEW SYDENHAM SOCIETY.

INSTITUTED MDCCCLVIII.

VOLUME XLVII.

MANUAL
OF
HUMAN AND COMPARATIVE
HISTOLOGY.

EDITED BY

S. STRICKER.

ASSISTED BY

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VOLUME I.

TRANSLATED BY

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THE NEW SYDENHAM SOCIETY,
LONDON.

1870.

TRANSLATOR'S PREFACE.

THE idea of translating Professor Stricker's "Manual of Histology" originated from a consideration of the remarkable paucity of works on this subject in our language. The only complete treatises we possess are "Kölliker's Manual of Human Histology," translated in 1853-4 by Messrs. Busk and Huxley. and again in 1860 by Dr. George Buchanan; the "Physiological Anatomy" of Messrs. Todd and Bowman, 1843-57; and the "Introduction to Quain and Sharpey's Anatomy," 1864-67. All of these works are extremely good; but that they should constitute the only books of reference on the minute anatomy of the tissues is certainly surprising when we call to mind the great multitude of works that have been recently published on the kindred subjects of Anatomy and Physiology. No doubt a large amount of valuable information is contained in Dr. Carpenter's valuable physiological treatises, and the various papers of Dr. Beale; but neither lay claim to constitute a complete exposition of histological knowledge; and, with the exception of these, the student who is desirous of referring to any histological point must go back to the short work of Morel, published in 1861; the "Lectures" of Quekett, 1850; the "Microscopic Anatomy" of Hassall, 1849, or some of the still older works on general anatomy, all written at a time when the methods of investigation were far less perfect than at present.

The translation of this treatise into English was commenced almost as soon as the first part appeared in this country; for it was felt at once nothing could give a stronger guarantee

that the several parts as they were successively published would represent the most recent acquisitions to our knowledge of Histology than the high authority of Professor Stricker and the names of the distinguished workers who had consented to co-operate with him in its production; especially as to the care of each of these writers was consigned the subject to which he had paid particular attention; and the translator was glad to find, after he had for some time been engaged upon it, that his own opinions respecting the merits of the treatise were concurred in by men who were so peculiarly qualified to judge as Professors Huxley and Turner.

The translation occupied nearly seven months, and the printing four; it is therefore only about one year behind the date of the original, and it is hoped that the second volume will be issued still more quickly after the appearance of the last part, which is promised in the autumn of the present year.

The translator had accumulated some material which he thought might be advantageously added in the form of an appendix, to show the progress that had been made in the different subjects discussed in the text during the past twelve months; but upon consideration it was thought better to omit them, and they will appear in a condensed form in the "Biennial Retrospect," to be published, as usual, at the beginning of 1871.

In conclusion, the translator may be allowed to add that he has endeavoured to give as faithful a rendering of the original articles into English as possible; and though conscious of occasional obscurities in diction, he trusts that the inaccuracies that may be found will be neither numerous nor important.

HENRY POWER.

SEYMOUR STREET, LONDON.
July 5th, 1870.

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INTRODUCTION.

GENERAL METHODS OF INVESTIGATION.

By S. STRICKER.

The microscope is a means of research. When objects are so small that at ordinary distances from the eye they no longer produce sufficiently large images on the retina, they require, for their examination, either a simple or a compound microscope. The domain of investigation embraced by this instrument, however, does not limit research. Microscopy defines no doctrine, but is simply a method of examination: yet it is the most delicate with which we are acquainted for terrestrial objects, because modern microscopes are the most perfect of all optical instruments.

Up to the present time the microscope has been chiefly applied to the investigation of the various organisms; and our knowledge of the finer structure of plants and animals, and especially of the latter, has assumed the character of an independent science, which again presents important subdivisions. The observation of healthy tissues, and of those modified by, or originating in, disease, already constitutes the basis of two separate but closely allied departments of science, each of which can again be regarded from different points of view. We can for example, push our inquiry either into the morphology or into the biology of the tissues; or, as it may be otherwise expressed, into the normal or pathological anatomy and physiology of the tissues. At present, however, the morphology and physiology of the tissues are so intimately connected with each other that no line of demarcation can be drawn between them. The observation of the vital phenomena presented by

the tissues, and the experimental investigation of their properties conducts us, in many instances, to a knowledge of the most delicate structural arrangements; whilst the converse always holds true, that a thorough knowledge of structure furnishes the key to many vital phenomena.

The technical methods of research applicable to these two subjects are nevertheless different. When we desire to follow, and ultimately to modify, the vital processes under the microscope, other means of research are required than when we merely wish to acquaint ourselves with the forms of the elementary parts. Moreover, experiments which are performed under the microscope differ according to whether they are conducted on living or on dead bodies. The sensitiveness of the former to external influences, makes—even in the microscopically small compass of the instrument, and bearing in mind the management necessary for its use—experiments possible under circumstances which are not practicable in the case of dead tissue. Thus we find that changes can be induced in living tissue by slight variations in temperature, by feeble currents of electricity, and by weak solutions of acids; whilst the operation of these agents must be much more energetic for the purpose of experiment on the dead body, and this is not always agreeable for the observer, nor suitable for the more delicately constructed instruments. The greater sensitiveness of the living organism demands proportionate delicacy in its treatment, but at the same time facilitates experiment; and to this we may ascribe the circumstance that experimentation on the living body has gained so much in value during the last few years, that is, during the period that the investigation of living tissues has been so extensively undertaken.

The tissues may either be examined by the light which they reflect from their surface, or by that which passes through them—by direct or by transmitted light. Every object can be examined by direct light, provided that the degree of illumination from without, and its own power of reflecting light, are sufficiently great, and that both the object and the instrument can be fixed.

It is self-evident that the instrument must be capable of being focussed, or it would be impossible for trustworthy reti-

nal images of various objects to be obtained. The examination of an object cannot be conducted by direct light with high powers, because the employment of such powers necessitates the close approximation of the lens to the object, whereby the latter is covered, and its illumination prevented. It is, however, possible to apply here the principle of the ophthalmoscope, and then this difficulty is overcome.

Examinations conducted by means of direct light are greatly assisted by direct illumination, or, what is still better, by throwing a pencil of rays on the part of the object to be illuminated; details then frequently become apparent which can scarcely be detected with the mere diffused light of day.

If examinations by means of direct light are undertaken at greater distances—as when, for example, lower powers are employed, or when the objects are examined or are prepared in a fluid—it is advantageous to use Brücke's doublet. This is placed in the arm of a Nachets' or Hartnack's stand, and the object is placed on the stage. The focussing can then be easily accomplished with the unassisted hand by moving the lens. This combination is very serviceable for preparations that have been teased out with needles, as in the isolation of ganglion cells and the separation of fine fibres. The object is in every instance placed on an opaque ground: if it be dark, upon a dull grey; and if clear, upon an opaque black ground. The object requiring to be isolated should in all instances be laid on a slide of polished glass, beneath which again may be placed a piece of dull white or black paper, as may be most convenient. For the examination of larger portions of tissue in fluid, little shells may be used, resting on a plane base, and having a spherical hollow, resembling an ordinary glass salt-cellar. A dull opaque ground may easily be obtained by covering the surface of the glass with a thick layer of coloured wax or gutta-percha, which has the advantage of enabling the objects to be fixed in position by transfixion with needles.

If it be required to bring the object into strong relief, in order to examine the details of the surface, the lenses of Steinheil of München are especially to be recommended. It is advantageous, however, to attach them to an arm moving on a ball and socket joint, which again plays, horizontally and ver-

tically, on a fixed vertical support. When it is required to manipulate with forceps and scissors under still higher magnifying powers, the little preparation cell should be fastened upon a blackened wooden block, several centimeters in height, and resting on the table. The arms being thus in a nearly horizontal position, and well supported, permit the observer to work with greater steadiness. In making preparations with strong lenses, the nose of the observer necessarily comes into close proximity with the object, and the bridge of the nose can be used as a point of support for the cutting instrument employed. When sections are made with scissors and forceps under strong lenses, it is usually necessary that the object should be firmly fixed, and, at the same time, very steady movement on the part of the cutting instrument is required. It is in particular quite indispensable that some kind of support should be given, if it be required, to make clean and thin sections of small and delicate objects.

If the left eye be applied to the lens, the right hand can with great certainty direct a fine pair of scissors balanced on the bridge of the nose whilst the left hand fixes the object. For the fixation of very delicate objects, substantial forceps, with very sharp, smooth points, will be found serviceable. If it be desired to work by means of direct light with a compound microscope, weak objectives, such as the No. 5 of Hartnack's microscope, or those corresponding to them of other instruments, can alone be employed. Formerly weak compound microscopes, which gave erect images, were used for the preparation of objects. These so-called dissection microscopes are not, however, really necessary, since the opposite movement of the hand demanded for the inverted image is soon acquired by practice.

The examination of objects can, in like manner, be undertaken with transmitted light, both with the aid of simple and of compound microscopes. In regard to the use of the former, there is little to be added to what has already been said. For the examination of objects with transmitted light, it is obvious that the support must be transparent, and the objects must themselves be illuminated by the reflected light proceeding from either a mirror or a prism. Simple micro-

scopes, or the lower powers of compound microscopes, can only be used with transmitted light, when general views of the topographical relations of the tissues to one another are desired. The larger the object, the lower must be the magnifying power employed, in order that a general view of it may be obtained. With such large objects it is usual to examine them in the first instance with a low power, and then to investigate the details of each part with a higher power. The very powerful lenses lately manufactured by Hartnack are extremely well adapted for the investigation of the living tissues, or of the well preserved and isolated elements of the tissues. In specimens which have been roughly treated and are consequently not in a very fit state for microscopic research, as in those that have been hardened with reagents, or stained with colouring matters, and repeatedly washed, very high powers are in the first instance less instructive than lower ones; indeed, those who are not very expert in the use of the instrument can actually see less with a No. 15 than with a No. 8 Hartnack. However, the highest powers are even here very serviceable to the beginner, if he be engaged in the definition of the deeper lying tissues. It is only requisite to use the fine adjustment with extraordinary care, to turn the screw with great gentleness; so that a fresh field is obtained, which may remain for some time under observation prior to passing to a greater depth, or returning to a more superficial part.

But if well isolated and well preserved morphological elements are under observation, and if the tissues are examined whilst still fresh, and without the addition of any fluids, or only of those which occasion no change in them, the highest powers prove of the utmost value. The advances that have been made in our knowledge of cells and of the finer structure of nerve fibres are the result of researches undertaken with the admirable instruments that have recently been constructed. The value of these high powers is strikingly illustrated by the investigations on the living cornea, conducted by Recklinghausen and Kühne. It is indeed true, that in the perfectly fresh state the structure of the cornea cannot be satisfactorily ascertained, even with the best glasses. In this state

only those morphological elements are to be distinguished which refract light differently from the surrounding parts, and thus it happens that when fibres or cells are imbedded in connective tissue, or in fluids, the refractive power of which is the same as their own, they cannot be perceived even with the best glasses, and artificial means must be resorted to in order to render them visible. These may either be mechanical, effecting the separation and isolation of the morphological elements, or chemical, which dissolve the connecting material, or act differently upon it than upon the morphological elements. The best artificially prepared specimens, however, cannot supply the advantages of examination made on fresh preparations with magnifying powers of from 1,000 to 1,500 linear. Those outlines which can be distinguished in the living tissue, exhibit, besides sharpness, a certain softness, which renders their definition easy and pleasant. The naturally present cavities and fissures, in consequence of the different refractive power of their contents, differentiate themselves from the surrounding material with extraordinary sharpness. Lastly, outlines are distinguishable during life, which completely vanish after death. Even if these can be again rendered visible by the application of peculiar reagents, their full significance is only to be recognised by our knowing that they are naturally present.

In the present condition of our instrumental means of research, it appears to be advantageous to commence histological studies by means of general topographical examination of the tissues with lenses of low powers; then to proceed to the examination of specimens that have been subjected to manipulation with lenses of moderate power, in such cases applying the stronger lenses only as a means of control for the penetrating powers of the weaker ones; and finally to proceed to the examination of the fresh tissues with the best means at our command.

I can attribute no very high value to the binocular (double tubed) stereoscopic microscopes, so far as their use has at present extended. As yet they have only been employed with low powers. The relief of different parts of an object can be very well ascertained, even with a simple microscope, by merely varying the inclination of the head.

The simplest, but at the same time the most certain and elegant, mode of investigation with the compound microscope is to place the object in the centre of a smoothly polished slip of glass, covering it with a thin quadrangular and also perfectly clean glass plate. The little glass plate, called also the glass cover, should lie with its surface parallel to the glass slide, a position which can only be attained when the object to be examined has been greatly and equally extended. Irregularly shaped and thicker masses interfere with the examination, because they make the glass cover assume an oblique position. If the tissue to be examined is diffused through a fluid, a drop should be placed on the glass slide; the cover should then be brought down to the upper surface of the drop, and cautiously allowed to fall by its own weight. By this means the inclusion of air bubbles is avoided. If the investigation is about to be continued for some time, or if it be desired that the medium in which the object lies should not become concentrated by evaporation from the edges, a brush dipped in oil may be drawn round the margin of the covering glass, which will effectually prevent it. If, after the glass cover has been applied, a portion of the fluid about to be examined exudes from the edges, so that the cover slips with an unsteady movement over the surface, a little piece of filtering paper may be employed to remove the excess of fluid, and the oil may then be applied. By this means the simplest kind of moist chamber may be made.

Recklinghausen first introduced the use of the moist chamber. The guiding idea of this was, that the object should be placed in a space in which the air was saturated with moisture, and this appeared to be so much the more important when it was found desirable to examine objects without a covering glass. In such cases the object is, of course, partially in contact with the air, and must necessarily give off watery vapour, unless the air be itself saturated with moisture.

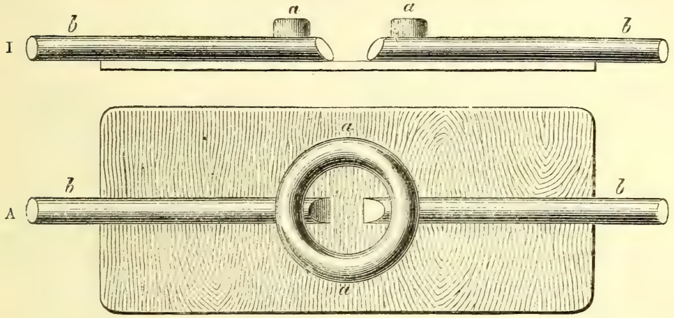
But if we consider, on the other hand, that the precipitation of watery vapour from an atmosphere saturated with it upon such an object is dependent on temperature, it is easy to understand how difficult it is to obtain the exactly intermediate point in which water is neither given off nor taken up

Any imperfections in this respect, however, will increase with the capacity of the space by which the object is surrounded. It should therefore be made as small as practicable, and, if possible, altogether dispensed with; in other words, where practicable, only a covering glass should be used, the edges of which are oiled. The pressure which this exercises on the object is unimportant, and may, indeed, easily be avoided altogether; for it is only requisite to form an outside wall with oil, and to place a small quantity of the fluid within the space thus enclosed, before applying the covering glass, in order to protect it entirely from the weight of the latter. Circumstances may exist, however, which render it necessary that the preparation should be exposed to the air. It may, for instance, be requisite to ascertain the influence of various gases; in these cases a chamber must be used, of as small a size as possible, except where some special arrangements are made, enabling the amount of watery vapour present to be regulated. I employ for this purpose a ring of putty, varying in thickness according to circumstances; the object is then to be attached, as usual, to the lower surface of the covering glass; this is now to be brought down upon the ring of putty, and to be gently pressed down on the object with the handle of the scalpel. A drop of water placed upon the slide is sufficient to saturate the space with aqueous vapour, and to prevent the object from drying. Great caution must, however, be used; for it will be found that the dry, smooth, polished covering plate becomes immediately tarnished when it is placed on the wall of putty. The drop of fluid should therefore only have a small surface, in order that it may not evaporate to too great an extent, and, on the other hand, it should not be too small, lest the object dry with too great rapidity. It is obvious that small variations in the proportion of water in the object are unavoidable.

A moist chamber formed in this fashion can easily be converted into a so-called gas chamber. In that part of the soft wall of putty which corresponds to the middle line of the glass slide, a small glass tube is to be introduced on each side, and to these caoutchouc tubes can be attached, which can be closed by bull-dog forceps when the passage of gas is not required. But when gases are to be transmitted, the necessary communi-

cations can be made through the caoutchouc tubes, and the forceps removed. This temporary and easily deranged chamber will not prove satisfactory to those who are constantly working with gases; by them it will be found better to cement the conducting tubules of glass once for all into grooves cut in the slide. The spaces left can be filled up with putty.

Fig. I.

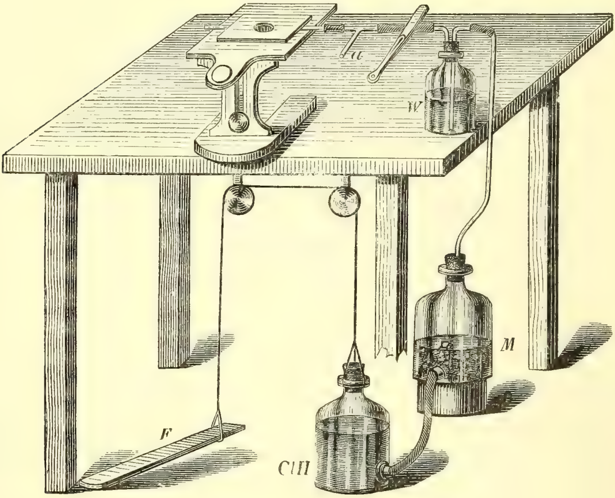


Gas chamber, natural size. A, bird's-eye view; B, longitudinal section through the middle line; *a a*, wall; *b b*, conducting tubes.

A slide which is to be used for such investigations with gas must be attached to the stage of the microscope, because the conducting tubes pull upon it, and so render the object liable to be displaced. The gas should be transmitted from washing flasks fixed on the stage, so that there may be firm supports between them and the microscope, whilst they are themselves connected with gasometers at some distance from the stage. In my own investigations, in order to be able to dispense with the services of an assistant, and use both my hands at the stage for microscopic purposes, I have arranged my gas apparatus beneath the table in such a way that I can effect the passage of gas in one direction or the other by means of a treadle. If, for instance, I wish to transmit carbonic acid gas, I so arrange the apparatus, shown in fig. II., that the flask containing hydrochloric acid gas can be raised by a string attached to the treadle, and passing over pulleys. From the evolving flask M a caoutchouc tube leads to my fixed wash bottle W, and from this another tube passes to the microscope. The con-

duction of carbonic acid to an object under the microscope renders it requisite that we should be able to exchange it at will for atmospheric air. I introduce, therefore, between the wash bottle and the slide a T-shaped tube (*a*, fig. II.). The horizontal portion of this tube lies in the axis of communication between the wash bottle and the slide; whilst the cross-piece is directed towards the observer. A long caoutchouc tube is attached to the latter, the end of which is seized by the observer between his teeth.

Fig. II.



Between the T-tube and the wash flask W, a clip is introduced. When I open the clip,* and by means of the treadle F raise the flask containing acid, and thus cause carbonic acid to flow into the wash flask, and at the same time compress the caoutchouc tube between my teeth, the gas must pass over the slide; but if I apply the clip, and inspire through the tube in the mouth, I then draw in free air from the opposite end of the chamber. By this arrangement common air can be exchanged

* The use of the clip may be dispensed with if the column of water in the wash flask is high.

at will for carbonic acid gas, without interfering with the observation, and at the same time the hands are left free for any manipulation that may be requisite. A second apparatus, the so-called DEVILLE'S, is arranged for the preparation of hydrogen beneath my table in the same manner as that above described. I use this gas as an indifferent medium; and as it passes through a wash flask, mingle with it various vapours, as those of ammonia, chloroform, etc. The mixture is accomplished by the aid of a bag, which can be compressed with the foot, and from which a tube conducts into the wash flask. If the effect of pure hydrogen gas is desired to be seen, the above-mentioned gas chamber is insufficient. Kühne, to whom we are indebted for making the first investigations with gas chambers, employs a mercurial valve. Adopting this principle, I take a slide made of hard caoutchouc, which is perforated in the middle, and to the surface of which a glass plate is cemented; or, which comes to the same thing, I take a ring of hard caoutchouc, and cement it to a glass plate. A groove is now made round the perforation, which can be filled with mercury. The cover glass must then be cemented to a little cell (fig. III. *b.*)

Fig. III.

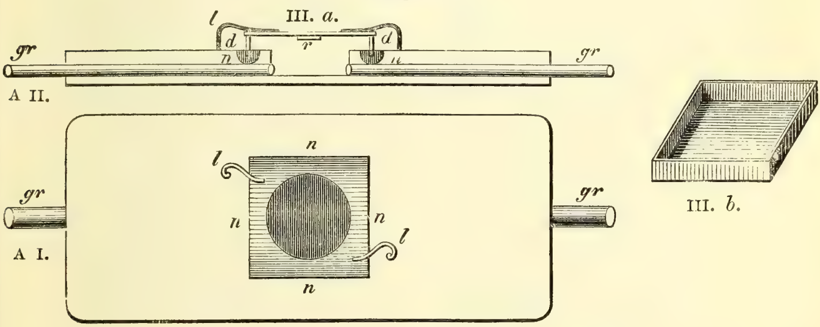


Fig. III. *a*, Gas chamber, with mercurial valve, natural size. A I, bird's-eye-view; A II, longitudinal section through the middle line; *n n*, groove; *ll*, clips; *gr*, gas tubes; *r*, object; *d d*, covering glass in section. Fig. iii. *b*, covering glass.

The object is placed on the inner surface of the cell thus formed, and the lateral walls of the cell are placed in the groove,

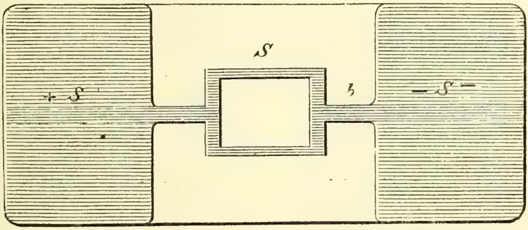
dipping, therefore, into the mercury. If the cover glass is now kept down by clips, the gas chamber will be perfectly closed; and no further explanation is required to show how the gas, whose effect is to be examined, may be conducted over the object.

There are certain difficulties accompanying the examination of objects in gas chambers; taking the simplest case for example, a drop of blood is placed on the lower surface of the cover, which is then laid on the cell, and firmly luted to it. The first current of gas which passes over it dries up the edges of the blood spot, and this can scarcely be avoided. It becomes necessary, therefore, to experiment with great rapidity in the gas chambers, or to add some indifferent fluid to the preparation, which may saturate the air contained in the little cell with aqueous vapour without essentially altering its character. But we are thus no longer working under the simplest conditions, and due allowance must be made for this in the conclusion at which we arrive.

The employment of the moist chamber is rendered still more difficult, if it be desired to warm the object whilst under observation with the microscope. Rollett was the first to introduce a means of varying the temperature in microscopic investigation. Max Schultze made improvements in this direction, and has constructed a stage capable of being heated, which can again be fitted to the stage of a microscope, is capable of being warmed throughout its whole extent, and can furnish the means by which the temperature of the object under examination can be varied at will. Various modes have since been suggested, by which the effects of elevation of temperature upon an object can be ascertained. In Max Schultze's stage, the mode of warming consists in the direct conduction of heat through metal plates. The attempt was subsequently made to conduct a warm fluid through the object stage, and still more recently, to employ warm vapour with the same object in view. A better method than any of these, and which demands attention as a means of heating the stage, consists in the conversion of a constant current of electricity into heat. In microscopical investigation, only a very small absolute quantity of heat is required, and indeed it is not necessary to

warm the stage in its whole extent, but only its centre; or, what is still better, the glass cover placed on a slip of caoutchouc. An amount of heat so small as this we may reasonably expect to obtain from the interruption of even feeble currents of electricity. It is well known that the heating of a wire, introduced into the arc of a constant current, increases with the diminution in diameter of the wire; and indeed, according to Riess, in the proportion of the bi-quadrate of the diameter. For this purpose, therefore, we employ a proportionately thin wire, attached to the centre of a glass plate, the ends being in connection with the electrodes of a constant battery. When the current is closed, the temperature of the centre of the glass plate is raised. The attachment of the wire presents, however, certain inconveniences; and we possess in tin-foil a more appropriate means at our disposal. I am accustomed to cut the tin-foil into the form represented by S in the adjoining figure, and then

Fig. IV.

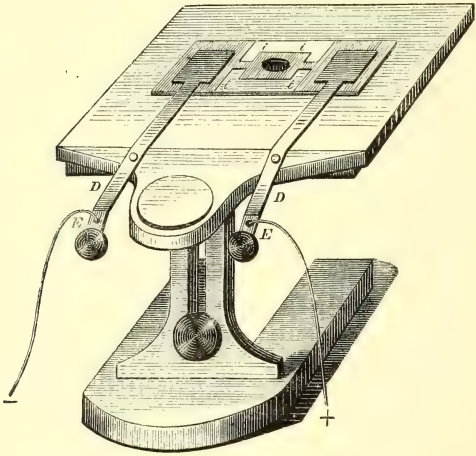


Slide adapted for being heated by means of electricity. Natural size.

to glue it to a glass slide; if now the extremities of the tin-foil are introduced into the arc of a constant current, the end in view is at once attained. A very convenient method of introducing the slide into the current is to attach to one of Hartnack's microscopes a couple of brass springs, by which the preparation can be firmly clipped. These springs (D D, fig. V.), which are attached to holes in the stage by means of brass pins, are provided also with india-rubber pins, by which means they are isolated from the microscope. When they firmly clip the slide, they at the same time press on the broad end of the tin-foil S. It is then only requisite to attach a conducting wire at any

point of each spring (E E, fig v.), and the circuit will be closed by the tin-foil. A second strip of tin-foil, of the same breadth as that attached to the slide (*b*, fig. IV.), is wound round the bulb of a thermometer, and introduced into the circuit at any convenient point. This furnishes the means of correctly estimating

Fig. v.



Foot and stage of one of Hartnack's microscopes.

the temperature attained by the centre of the slide, when all the secondary conditions are uniform. These latter can, however, be estimated by comparison, and the due employment of a thermometer,—a proceeding that is always requisite, whatever may be the mode of heating employed. In order to accomplish this, at the point where the object is situate, a fatty substance, the melting-point of which is known, should be placed, and the reading of the mercury should be taken at the moment that the fat begins to melt. The quantity of fat that is introduced should be very small, and should be in the field of the microscope. It will be found most expedient to cut a little disk out of the fat, to cover it dexterously, to watch it with a lens, and to calculate it accordingly.

I also apply one of Meidinger's chains with amalgamated zinc plates. A chain of this kind works with very great

steadiness, if fed with regularity. It can be left closed for several days, and yet the temperature of the tin-foil kept to a definite degree, not varying with that of the room. It seldom requires water, but crystals of copper must be supplied at least once a day, so that the solution may be constantly and equally saturated. If we overlook, however, these slight drawbacks, and reflect that such precautionary measures are only requisite in cases where it is wished to maintain a particular preparation at a uniform temperature for many days and nights, we shall feel that in the interest of such important investigations it can scarcely be thought too great a trouble to attend at least once a day to the requirements of the machine. If the amount of work performed by the battery be but small, or if it be only occasionally applied, it will then long retain its activity without requiring other addition than that of a little water from time to time to supply the place of that which is lost by evaporation.

Meidinger's arrangement gives off no injurious vapours, and may therefore be enclosed in a little box, and placed beneath or near the work-table. I transmit the conducting wires through holes bored in the table, and when required for use, fasten them to the points indicated by + and − in fig. v.

Inasmuch as the temperature of a thin wire introduced into a thicker arc is inversely as the square of this wire, whilst its length, when small, is of no importance, it follows that the method of measurement formerly employed is justified. But it is also clear that the active force present can be accurately accommodated on the basis of this law. For if the temperature diminishes as the square of the strength of the current, this decrease can, to a certain extent, be covered by diminishing the transverse section of the tin-foil, so that if a weak current be in use, the strip of tin-foil must be made proportionably narrow. As these strips are easily torn, I am accustomed to glue the tin-foil upon thin paper, and then cut out a very long strip with its central window. The larger portion of the strip I twine round the bulb of a thermometer in such a way that after making several coils, the two ends hang free. I then, cover the whole bulb with a layer of shellac or glass cement, and pass it through a cork into an empty vessel, so that the ends of

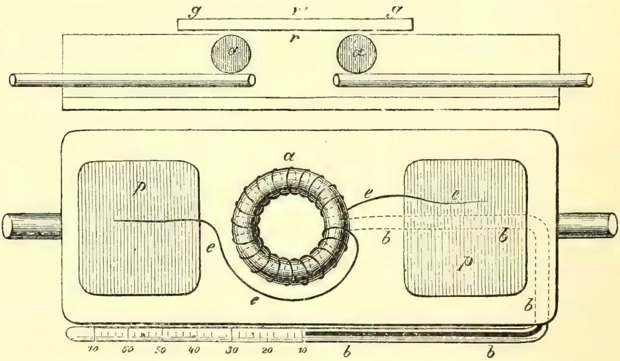
the tin-foil project. No special expertness is then required on the part of the experimenter to introduce these into the arc of the current. The bulb can also be so placed in front that its readings can be readily taken. The shorter end of the strip of tin-foil, with the window, I place as is shown in fig. VI. In my arrangement, the temperature of the strip of tin-foil rises in almost arithmetical proportion to the number of elements used,* when these are so arranged that each zinc is connected with a copper pole. With one element, and the arrangement just described, I obtain an elevation of temperature amounting to about 5° C (9° Fahr.), and with six elements rather more than 30° C (54° Fahr.). If great accuracy is required, the regulation of the temperature must be accomplished by means of a rheostat.

In order to exercise a direct control over the temperature of the glass cover, I attach a thermometer to the slide itself. In

Fig. VI.

A II.

A I.



Gas chamber, with thermometer, capable of being heated by means of a constant current.

fig. VI., a represents the flattened bulb of the thermometer, whilst the dotted line b indicates the direction of the tube. Both the

* It must be expressly understood that the ratio here given corresponds only to a certain definite arrangement. It follows from Ohm's law that the resistance of the introduced strip governs this ratio. The strength of the battery required must be ascertained by experiment.

tubes and the bulb lie in a groove made in an india-rubber slide. A coil of very fine copper or platinum wire is wound round the mercurial bulb *a*, and the ends are made to lie on the broad metal plate *p p*. The springs which conduct the current through the instrument press upon these plates.

Fig. VI. A II. is a longitudinal section of the stage in full working order; *g g* is the little glass cover, upon or to the under surface of which the object to be examined is attached. The cover is in contact, not only with the surface of the slide, but also with the coil of wire surrounding the bulb of the thermometer, the transverse section of which is seen at *a a*. When the circuit is closed, the wire becomes heated, and acts on the one hand upon the mercury, and on the other upon the cover. The hard caoutchouc is a bad conductor of heat, and hence the cover receives the greater part of the heat. The figure renders it apparent, also, how the slide can be at the same time used as a gas chamber.

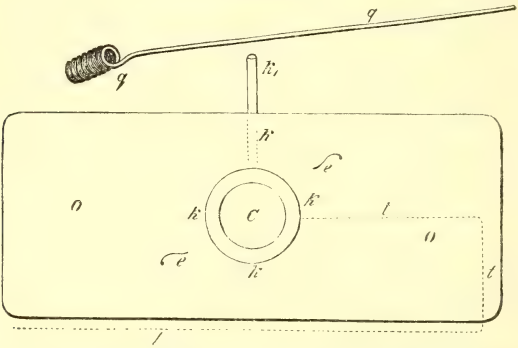
Where only the centre of the slide, or the cover, is desired to be heated, the flame of a candle or gas jet may be conveniently employed as a source of heat.

For this purpose a copper ring and rod of the form *kkkk* fig. VII. are so inserted into the glass slide *o o*, that they do not project beyond its surface; when it is required to be heated, the rod *q*, with its coil, is slipped over the free end K K, and to the extremity *q* the flame, which should be as small as possible, is applied. If the rod is of about the thickness of a large knitting-needle, it can be made of sufficient length to obviate any inconvenience to the observer from the flame. The centre C of the slide must be accurately arranged for a particular object glass, flame and focus. If a very small one be employed, we may reckon upon tolerable uniformity of temperature being maintained, though of course this mode has no pretensions to scientific accuracy. If, however, the general effect of an increase of temperature within certain limits is all that is required, it is sufficiently useful. The facility with which it can be made renders it valuable for large laboratories.

I have constructed another slide with a thermometer attached, on the same principle of heating. The thermometer is fashioned, as in fig. VI., in the form of an arch, and is imbedded in

a plate of caoutchouc. The bulb, however, is not surrounded by a spiral, but by a metal shell, which resembles *k k k* in fig. VII., and to this the projecting rod *k′* is fastened. If the apparatus represented in fig. VII. is imagined to be made of ebonite, and perforated in the centre, the dotted line will represent the position of the tube of the thermometer. Inasmuch as the object must in every case be placed on a covering glass, two clips (*e e*, fig. VII.) are added to fix the glass. If the

Fig. VII.



Slide capable of being heated, represented of natural size. *k k k k*, copper ring and rim imbedded in the plate *o o*; *q q*, heating rod; *e e*, clips.

plate is to be used as a gas cell capable of being heated, the object must be placed on the lower surface of the cover; but if only as a slide capable of being heated, it must be placed on the upper surface, and requires then its own cover. In the latter case the lower cover (*g g*, fig. VI. A II.) is equivalent to the ordinary slide, and only possesses the advantage of being a thin plate, the temperature of which can be easily raised.* The disadvantages of an ordinary gas cell appear prominently in the cell capable of being heated. In no arrangement with which we are at present acquainted does an equipoise between the preparation and the atmosphere surrounding it occur. The

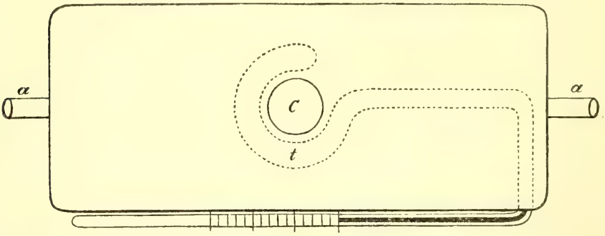
* The mechanician, Heinitz, in Vienna, has constructed a gas cell capable of being heated on the model of that just described, with a degree of elegance that leaves scarcely anything to be desired.

temperature of each part of the cover changes as the object glass sweeps over it, and must necessarily vary within certain limits, even with the best means of regulating the temperature. Each time that it is cooled, a precipitation of the watery vapour from the atmosphere that is saturated with it must occur. Recklinghausen and Kühne have endeavoured to obviate this inconvenience by the construction of a more complicated apparatus for supplying heat. Whilst the results of these experiments are still unknown, it is advisable to postpone the investigations on the effects of heat in the gas cells. The reason that has induced me to describe the construction of the heatable gas cell at so great a length is, that it affords excellent results in quite another line of inquiry. If the floor of the cell be covered with a drop of water, and the preparation is attached to the under surface of the cover over the water, all increase of temperature will cause the atmosphere within the cell to contain more watery vapour, of which a part will condense on the object. If a delicate test object be examined, such, for example, as the blood corpuscles constitute for a practised observer, it will be remarked that every addition to the temperature produces a perceptible alteration in the object, attributable to the increased proportion of water in the serum. We thus possess the power of supplying water, in very precise proportions, to preparations enclosed within a cell.

It has been further ascertained that the action of gases on blood is different in accordance with the amount of water that it contains. The results of the experiments that have been hitherto made will be detailed in the chapter on the blood. A single example may, however, here be given to show the advantage that gas cells capable of being heated can afford. It may, in some cases, be very desirable to be able to vary the temperature within certain limits with rapidity. I have, indeed, had occasion to perform some experiments in which it was requisite to pass, alternately, iced water and steam through the cell. For this purpose I have constructed a metal slide, in which a central perforation (C, fig. VIII.) permits the passage of light; and the preparation may again either be placed upon a glass cover cemented down, or may be so arranged that the hole in the slide serves as a cell. The plate itself must consist

of two leaves, so separated as to allow an evenly enclosed space to exist between them. Then, at opposite points of the space, two small tubes are inserted (*a*, fig. ix.) To one of these an india-rubber tube *b* is attached, which leads to the vessel for generating steam F. This consists of a flask, through the cork of which a rectangularly bent glass tube is transmitted. The free end of this tube must now be brought into connection with the slide; in this communication a T-shaped tube is again introduced. A lamp with a small flame is placed beneath the flask,

Fig. VIII.



Metal slide for the conduction of water and steam. *a a*, conducting tubes; *t*, thermometer.

which is half filled with water, so as to keep up gentle ebullition. The steam escapes through the perpendicular limb of the T-shaped tube, because it here meets with the least resistance. When, however, this is prevented, which is easily accomplished by means of a caoutchouc tube and a clip, the steam passes through the slide, and heats it. If the lamp is now removed, the cooling flask exerts a suction power on the vapour in the space between the two leaves of the slide, and atmospheric air consequently enters; or if a receiver containing iced water be already prepared, this also may be sucked up, and rapid cooling effected. The temperature is ascertained by the thermometer, which occupies the position shown in the figure.

Electricity is also an agent of considerable importance in microscopical investigations. Brücke, in his physiological inquiry into the tissues, employed a slide covered with tinfoil, as shown in fig. x. The slide S S was placed on two

copper supports K, which were attached to the stage P. The electrodes were fastened to the supports, and the object was brought between the points of the lamina of tin-foil. The mode already described of obtaining and transmitting a current for the purpose of observing the effects of heat, will also, of course, serve for observing those of electricity. When this is the object in view, the slide should only be covered on its surface with tin-foil, in the form represented in fig. x. The springs resting on ebonite rods will serve as conductors. The distance of the laminæ of tin-foil from one another is of importance in regard to the transmission of the current. As a general rule they should not be separated from one another to a greater extent than a few millimeters. I prefer to see the two electrodes at the sides of the field, because then the position of the object in regard to them, and to the middle line, is simultaneously visible. It is a matter of very great moment to observe and distinguish between the effects of the current in the immediate neighbourhood of the poles, and at some distance from them; for the effects of electrolysis are produced on breaking the current in the vicinity of the electrodes, and the tissues become altered as they would be were they subjected to the action of weak acids or alkalies.

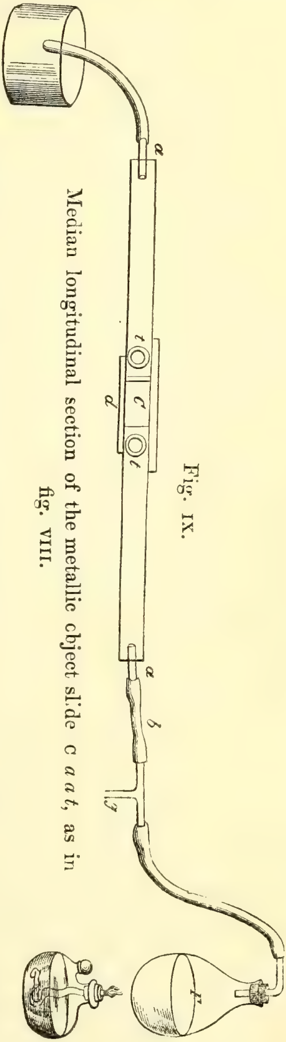


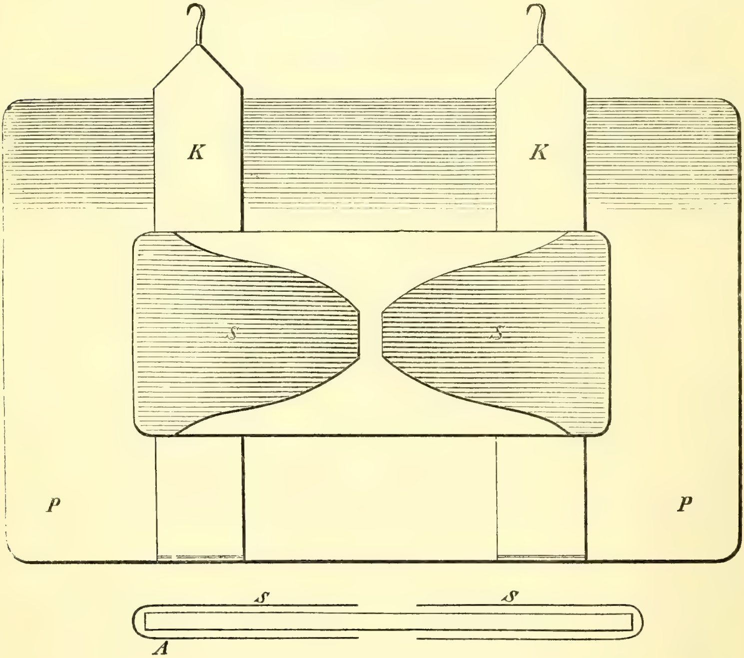
Fig. IX.

Median longitudinal section of the metallic object slide C *a a t*, as in fig. VIII.

At parts more remote from the electrodes changes also occur,

which, however, are not so remarkable as those which are induced by the chemical processes above alluded to. The effects which may be trusted as being really due to electricity should occur quickly after the passage of the current, and not be limited to the part in the immediate neighbourhood of the electrodes. If the current be allowed to pass for some time, that is to say, for more than a few seconds, through the tissue,

Fig. x.



the products of electrolysis first extend over the whole surface lying between the electrodes, and then the intensity of the current becomes extraordinarily reduced, frequently, indeed, to zero, on account of the pole becoming covered with bubbles of gas. On this account the employment of constant currents for microscopic investigation is scarcely to be recommended, for with the closure of even very weak currents, so violent a

development of gas occurs, that but little confidence can be placed in the results that are observed to follow their passage. The amount of electrolysis that occurs with induction currents is much smaller, and they have therefore been most generally employed. The arrangement in which there is a single shock on opening and closure of the current is particularly advantageous. The shocks obtained from a Leyden jar are infinitely superior to the constant currents, because the instantaneity of the shock causes the disturbing influence of the evolution of gas bubbles to be altogether abolished.

It is not practicable to carry out the examination of tissues, under the influence of electrical currents, with the same elegance of detail as can be accomplished when a simple slide only is employed. The single circumstance that the tin-foil, in adhering to the glass, makes the surface irregular and uneven, renders it necessary that the sections of the preparation should be thicker, and proportionately interferes with the investigation by means of high powers. I endeavour, therefore, to combine my researches with electrical currents, with those conducted in the gas cell. By this means I am able to avoid the inconvenience alluded to: for if the cavity of a slide, adapted as described above for a gas cell, be surrounded by a layer of soft cement, it is quite possible to place the electrodes in close proximity with the preparation which is on the inner side of the cover, and to examine it in consequence with high powers. I attach to each side of the slide a strip of tin-foil

Fig. XI.

which passes over the putty, and reaches its inner side (*s s*, fig. xi.) Cemented to the cover are also two small strips of tin-foil (fig. xi., *s′ s′*), which, running in the axis of the cover, leave between them a space of a few millimeters in diameter. The object is placed at this spot, and the cover is so disposed on the wall of putty that the metallic strips of the cover lie on the strips covering the putty, and the cover is then firmly pressed

down on the soft putty. The cell being now complete, the electric current is conducted by the strips of metal to the object, through which it passes at the same time; this lies immediately beneath the cover, and can therefore be examined with the highest powers. It is, moreover, no small advantage to combine the application of electricity with researches on the influence of gas, because we can neutralize or aid the effects of the current by the introduction of different gases.

On breaking the current, heat is developed in the tissue. I have measured the amount thus set free in my arrangement of the induction current, and find that it amounts, when the core is fully thrust down, to about 3° C. ($5\frac{2}{5}$° Fahr.) If an uncovered drop of blood is under examination with strong ordinary lenses, these become dimmed at the instant of the passage of the current, but after a short period they again become clear. The preparation, however, very soon dries up. It is requisite in such cases to determine what are the effects of the sudden elevation of temperature, and what are those of the electric current alone. An additional means of research consists in effecting a change in the fluid components of a microscopic object. We have not as yet been able to succeed in combining this mode of investigation with the application of gases. A reliable experiment in which an alteration in the fluid is effected is only practicable when the object is placed between the slide and the cover, the borders of which at two opposite points at least have not been oiled. To one of these points a strip of filtering paper with sharply cut edges should be attached, and at the other the fluid which is to be applied may be introduced by a small tube, one end of which has been drawn out into a long point. When the strip of filtering paper is attached to the side of the cover, it sucks up the fluid of the preparation: a current is immediately established, which as a general rule carries everything off that is not firmly adherent. If a little time is now allowed to elapse, it is possible by the cautious application of a very small strip to cause a slow and feeble current to pass over the superficies of the preparation whilst the deeper part remains at rest. If at any time the fluid is altogether withdrawn, the cover sinks until the deepest layers of the solid elements which cling to the cover are pressed flat, unless, indeed, they are too resistant to

permit of such compression. As often, however, as a fresh drop is supplied from the other side, the cover again rises. In such experiments the focussing screw of the microscope must be deftly handled, if it be desired to keep the attention fixed on any given object. By the foregoing method a microscopic object can be washed in a chemical sense. Living morphological elements bear such an operation only so long as the fluid supplied is of an indifferent nature. The operation of washing can, however, be more freely performed in the case of dead tissues, to which, also, water and various reagents can be alternately applied.

The formed elements may even be killed whilst under observation, and be then submitted to further reactions.

Water may be transmitted so as to allow it to be seen how young cells become spherical, and how a dancing movement of the granules in their interior occurs, how the nucleus becomes more clearly visible, and how they ultimately burst. On the application of acids, again the definition of the nucleus may be seen to become sharper, followed by the shrivelling of the nucleus, whilst the material which surrounds it loses its well-defined contour, becomes paler, and gradually disappears. Formed elements with hard outline can be seen to swell up on the addition of alkaline solutions. Lastly, dissolved colouring matter may be introduced, and the gradual process of coloration of the formed elements or of certain constituents of the preparation may be witnessed.

Preparation of Tissues.—If the constituents of the tissue—that is to say, the formed elements—do not form a solid mass, but only a loose texture with larger or smaller interspaces between them, no special preparation is required for their examination. A small quantity is placed upon the slide, and covered with a plate of thin glass. If the formed elements are in too close juxta-position, a drop of fluid may be added. It is to be borne in mind, however, that it is impossible to say of any fluid that it constitutes an indifferent medium for fresh tissues of all kinds. In all instances we must be prepared for changes taking place. Amongst those fluids which are most indifferent are, the fluid of the aqueous humour, the serum of

blood, and amniotic fluid in which a little metallic iodine* has been dissolved—the so-called iodized serum; finally, very diluted solution of neutral salts may be particularly recommended. If the formed elements have been already modified in their chemical characters by the addition of other reagents, if, for example, they have been soaked in a dilute solution of bichromate of potash, or of chromic acid, water alone may be added. Reagents which induce coagulation of the formed elements, and a consequent hardening of the tissues, cause them also to become cloudy. In order to examine such changed elements with any advantage by means of transmitted light, it is customary to apply highly refractive fluids, which, when they penetrate into their interior, render them transparent. The employment of these means have led to very remarkable advances in microscopic art.

The highly refractive medium must be soluble in the fluid in which the tissues had previously been macerated. Glycerine is a highly refractive liquid of this nature, and it is soluble in water. Tissues can therefore be removed from watery solutions and immersed in glycerine, or what comes to the same thing, glycerine may be directly employed as a fluid for mounting microscopical preparations. Oil of turpentine is still more highly refractive, but it is insoluble in water. A tissue cannot therefore be removed from a watery solution into oil of turpentine. But alcohol is soluble both in oil of turpentine and in water. If, therefore, it be desired to impregnate a tissue with oil of turpentine, it is first removed from its watery solution into absolute alcohol, and from this into the turpentine. In cases where the tissue forms a membrane, it is only requisite to spread it out when fresh; to add a drop of some indifferent fluid, and then to cover it with a plate of thin glass. This plan, however, is only feasible when the membrane is not too thick.

As a general rule, fresh tissues are more or less transparent, but after death they become cloudy. When, therefore, dead membranes are spread upon the slide, and are required to be

* The amniotic fluid should be pure and almost destitute of smell. A trace of putrefaction renders it less available. The addition of iodine colours the fluid of a feeble yellow tint.

examined with transmitted light, it is necessary, unless they are extremely thin, to add some highly refracting fluid. In the so-called parenchymatous organs—as the liver, spleen, and others—in the parts of the central nervous system, and in bones—nothing is usually to be seen, either in the fresh or in the hardened condition, so long as the connection of the morphological elements is not disturbed. It is requisite, in such instances, either to tease out small portions with needles, or to cut very thin sections.

a. THE PREPARATION OF SPECIMENS BY TEASING.—Specimens may be prepared in this way on the slide, a very small quantity of fluid being added: A minute fragment of the tissue should be placed on the drop, and then seized and torn by two sharp needles. Fibrous tissues can then be unravelled, as far as the vision of the observer and the optical means at his disposal will allow. The breaking up of tissues in this way is, however, accomplished, as a general rule, with less ease when fresh than after they have been macerated. The connecting substances which unite the formed elements are frequently of too firm a consistence to allow of their being thus torn, and the latter, therefore, are the first to yield, so that it is rare to see the formed elements whole and perfect. In such cases it is expedient to macerate the tissues for some time, in order to effect the solution of their connecting material. Solutions of potash have been applied, with this object in view, as well as of hydrochloric acid, bichromate of potash, Müller's fluid, and very recently, with excellent results, iodized serum. Lime or baryta-water is to be recommended for the isolation of the fibrils of connective tissue, whilst for the separation of the fibres of transversely striated muscles the tissue should be macerated in very dilute sulphuric acid, at a temperature of 40° C.; or it may be boiled in a mixture of chlorate of potash and hydrochloric acid. The most delicate manipulation of all is required for the isolation of nerve cells and their processes.

b. THE PREPARATION OF SPECIMENS BY SECTION.—It is only in some rare instances that sections can be made of animal tissues, either when fresh or after maceration, of sufficient deli-

cacy to allow of examination with moderately high powers. Teeth, bone, and cartilage constitute, however, exceptions to this statement. Bone can, even when fresh, be cut into thin disks with saws, which may then be rubbed down with emery on a roughened glass plate, and polished on a hone. Cartilage requires no preparation, as thin sections may be readily cut from it with a sharp knife. The teeth are too brittle for the application of a saw. They should be attached to a cork by means of shellac, and rubbed down upon a whetstone. As a general rule, artificial methods of hardening the tissues must be employed. The simplest and most elegant mode is that of refrigeration. The tissue to be examined is placed in a little platinum capsule, and imbedded in the freezing mixture; then, as soon as it has become hard, sections may be made with a cold knife. A second method of hardening that is in constant use is that by means of alcohol. The tissue, divided into small pieces, is placed in a flask containing absolute alcohol, which is renewed every few days, according to the amount of water present in the object. For membranous tissues, boiling in vinegar was at one time adopted, but so many better plans are now known, that it has with good reason fallen into disuse. If it be desired to harden the tissues by boiling, the best fluid is one which consists of eight parts of water, one part of creosote, and one part of vinegar; in this the tissues should be allowed to boil for two or three minutes, and be then laid out to dry. After two, or at most three, days it acquires a consistence which is admirably adapted for permitting sections to be made. The thin sections should then be treated with a little dilute acetic acid, in which the tissues again increase in volume, and they can then be examined either in water or in glycerine. If boiled preparations remain for a long time uncut, they gradually acquire such consistence that they are no longer appropriate for obtaining sections. This inconvenience has led to the method of drying. It is, indeed, much more advantageous to dry fragments of tissue. It is to be remembered, however, that the morphological elements of the tissues, in all these modes of hardening, are not so perfectly preserved as when they are kept in fluids. A means of hardening, of very general value and application, is found in chromic acid. This

should be applied in solution, containing 0·25 to 2 per cent., and the perfectly fresh tissue ought to be placed in a large volume of the acid solution. The skin and all mucous membranes, the intestines, bladder, and conjunctiva, become in the course of a few days sufficiently hard to permit sections to be made; and even this period can be shortened by removing the preparation from the chromic acid solution, and immersing it in alcohol, where it may remain for twenty-four hours. The proper hardening of the brain and spinal cord, however, requires a longer time. Large portions generally putrefy in the centre, though they harden at the surface. These parts of the nervous system should therefore be cut into small fragments. Here also the subsequent application of alcohol proves of great service. The bichromate of potash acts in the same way as chromic acid, but much more slowly, the effect produced in a few days by the latter requiring weeks with the former. At the same time, the bichromate of potash possesses the very great advantage that the tissues saturated with it do not become friable. Recently, perosmic acid and chloride of palladium have been recommended as means of hardening, the solution containing from one-fifth to one-tenth per cent.

Various forms of apparatus have been constructed, by means of which fine sections can be made. It would be undoubtedly a great step in advance, if they could be made in any way which would render us independent of manual dexterity. But up to the present time these mechanical means have not attained sufficient excellence to lead to their general adoption. Sections are therefore still always made by the hand, and their beauty depends on the greater or less skill of the operator. The knives employed should always be of the best quality, and extremely sharp; scalpels will be found to be best adapted for objects that have been hardened by boiling, whilst large flat blades are more appropriate for those that have been hardened in fluids. The sections, when made, may either be examined without further addition; or they may be first prepared by means of needles, or be freed from adhering or imbedded morphological elements by the frequent use of a soft brush, or by blows with a delicate rod, or by shaking them in small test tubes. If the tissues are friable, or too small to be seized

by the fingers, or possess a cavernous structure which it is desirable to preserve, or if they present irregularities and projections of the surface, like villous processes, or papillæ, and sections of these are required, the best method of dealing with the specimen is to imbed it.

The process of imbedding consists in dipping the tissue into some liquid which will easily set, even at the ordinary temperature of the air. For this purpose we may employ, first, a mixture of wax and oil, and secondly, a concentrated solution of gum. The first is prepared by melting oil and wax, in equal proportions, in a porcelain capsule, by the heat of a lamp. The proportions of the two substances can, of course, be varied; and, according to the peculiarities of the case, whether it is required to be a little harder or softer, more wax or more oil must be added. The piece of tissue which is to be imbedded should first be kept in alcohol for a length of time sufficient to cause it to be thoroughly impregnated with that fluid, or, perhaps more correctly speaking, till the water it contains is as far as possible removed. This will occupy a longer or shorter period, in proportion to the strength of the alcohol; with absolute alcohol, and with small pieces of tissue, a few minutes are sufficient. The specimen is then to be placed in pure oil of cloves, which is far preferable to the oil of turpentine, that at one time was so generally used, partly on account of its more agreeable smell, partly because it is not so volatile, and partly also because it produces a consistence in the preparation more favourable to the obtainment of firm sections. The specimen must remain in the oil of cloves till it is transparent, the infiltration of the oil being incomplete so long as any opaque spots remain visible. A little cone of paper may then be prepared, which is to be filled with the mixture, and into this the specimen is placed, whilst it is still fluid. Before the mass cools, the position of the object should be noticed; and when it has become firm and opaque, its situation may be indicated by a mark on the surface of the wax, through which, when perfectly cold and hard, the section can be carried. The section must be floated off from the knife. Imbedding is best adapted for very delicate objects, which have little consistency, and which cannot well be seized with forceps or needles. A portion

of the wax will always be removed with the section, and this must be detached from the knife by the aid of a little turpentine; the preparation will then float off, and may be placed upon the slide, or in a little cell, without further trouble.

If the preparation is to be subjected to no further manipulation, it is floated on to the centre of a slide, the superabundant fluid removed with care, and a drop of Canada balsam applied, after which a cover is placed upon it. The preparation is by this means completely preserved, and can be kept in this state and fit for examination for years. The process of imbedding in gum requires greater attention to minutiæ; but it is appropriate for specimens which contain much connective tissue, and answers for them much better than imbedding in wax. The preparation need not be impregnated with oil. It may be macerated for twenty-four hours in alcohol, of ordinary strength, and from thence be removed into a paper cone filled with a very concentrated solution of gum; the whole cone must then be immersed again in alcohol. In the course of two or three days the gum acquires a consistence which renders it very fit for making sections. No definite statement can be made in regard to the degree of this consistence, since it must be proportionate to the hardness of the tissue. Better sections are made of very soft tissues when they are imbedded in a mass which is not too hard, and *vice versa*. The sections may be floated off by means of a little water, and be examined after the addition of a drop of glycerine; or they may be subjected to further manipulation. In the former case, if it be desired to preserve the preparation permanently, the excess of glycerine is to be removed from the edges of the cover, and these may then be painted with a layer of varnish, which hardens on exposure to the air. For this purpose a solution of asphalt in turpentine, the so-called asphalt varnish, or some similar material, may be employed. The preservation of preparations in glycerine exerts no prejudicial influence upon them, and when it can be used it is preferable to Canada balsam. Sections which have been taken out of water may, however, be placed in alcohol, then in oil of cloves, and from thence they may be removed to Canada balsam, in which they may be preserved.

The contours of morphological elements, not previously

visible, can often be made evident by treating the preparation with certain colouring matters. The principle of this means of research consists in the circumstance that various constituents of the tissues become quickly stained with colouring matters, or combine with them, whilst others do not. The tissues should be dipped in the solutions of the colouring agents, allowed to remain in them for some time, and then washed. *Cæteris paribus,* the concentration of the solution stands in inverse relation to the length of time required in order that certain effects should be produced. It is therefore advantageous to use very dilute solutions, and to prolong the time of their action. The more gradual this is, the more scope is afforded for exact researches.

A division of the colouring reagents can be made—first, into those, the solutions of which, when examined by transmitted light, show the same absorption colours they impart to the tissues; secondly, into those which impart to the tissue one of their own proper absorption colours; and lastly, into those whose solutions absorb no definite colour, or are, as we are accustomed to say, colourless.

In the two last-mentioned cases, after saturation with the fluid, some chemical process must take place. An example of the first kind is seen in carmine, the alkaline solutions of which impart their own colour to the tissues; an example of the second kind is met with in chloride of gold, the solutions of which are pale yellow, whilst the tissues that are saturated with it assume a violet tint; and an example of the third kind is found in nitrate of silver, the solutions of which are colourless, but yet stain the tissues of a dark brown hue. The secondary chemical change may either occur without further addition, or some means must be employed to induce it. When the tissues are macerated in dilute solutions of perosmic acid, they assume, sooner or later, according to their chemical nature, a black colour, without any addition; but those which have been in solutions of nitrate of silver require exposure to light before the chemical change, which consists in the precipitation of silver, will occur. Gerlach introduced the method of examination by staining the preparation into practice. His first experiments were made with carmine. At the present

time, however, many colouring agents are employed; specimens may be stained with tincture of saffron, with anilin, with indigo-carmine, hœmatoxylin, and picric acid; and also with nitrate of silver, chloride of gold, chloride of palladium, and perosmic acid.

When fresh membranes are to be acted on by nitrate of silver or chloride of gold, the pieces should be cut from the living animal, and thrown into the solution without further preparation. The solution should be kept in a dark place as long as the action is allowed to proceed: the preparation should then be recovered by means of sharp-pointed glass rods, washed, and placed in the light.

After fragments of tissue are taken out of solutions of silver, they may be placed in alcohol or glycerine, and then exposed to light; or the specimen may be prepared for microscopic examination in glycerine, and allowed to remain in it for twenty-four hours. Preparations which have been in solution of chloride of gold, after having been thoroughly impregnated with it, should be placed in water slightly acidulated with acetic acid.

If the action is required to be more intense, the membrane is to be well brushed, before it is removed from the staining fluid, with a wet brush. This is the best method of procedure, for example, with the centrum tendineum of the rabbit, which should be thus brushed both on the abdominal and on the thoracic surface, whilst the cornea need only be brushed on the anterior surface, and then removed from the liquid.

In non-membranous tissues, just as in those which require to be broken or cut up for microscopical examination, the prepared specimen may be tinted whilst on the slide, after which it may be washed, and then covered in the usual manner.

Solutions of colouring matters which only act on the fresh tissues, as, for example, nitrate of silver, can obviously only be applied to sections made from recent and therefore necessarily frozen tissues. On the other hand, colouring agents which, like carmine, do not affect the fresh tissues, can only be applied to sections which have been made from dried specimens, or from those which have been hardened by chemical reagents. The particular mode of treatment adapted to each tissue will be

described in the several chapters devoted to the consideration of each. The results obtained depend very much on the measures adopted, though it was thought it would prove of advantage to give here a general account of them.

Besides the mode of staining the tissues effected by dipping them in various solutions, another may be mentioned in which coloured fluids are injected into the vessels. Formerly injections were only made with the object of rendering the lymph or blood-vessels visible by means of coloured material, and the structure of the vascular walls was wholly disregarded; but in the present day injections are made with the object of exhibiting the structure of the parietes of the vessels. For this purpose, for example, a solution of nitrate of silver may be injected. Where, however, a solution of this kind is employed, the tube which is introduced into the vessel, and termed the canula, must be made of glass or platinum, and be connected with the syringe, which should be constructed of the same material, by means of an india-rubber tube.

Instead of the syringe, an apparatus may be applied in which the injection fluid is propelled by the pressure of air. This mode of injecting, first introduced into practice by Ludwig, is far more certain and elegant than the old method of the syringe. The injection fluid is, once for all, placed in a Woulf's flask, the size of which is appropriate to the quantity of fluid required to be used. Into one neck of the flask a tube is inserted air-tight, and reaching to the bottom, the upper extremity of which is bent at a right angle, and drawn out into a point: the other neck of the flask is surmounted with a short and also rectangularly bent tube. When this is connected with an apparatus from which air can be driven under a definite pressure, the injecting fluid must be expelled from the opposite tube. If, now, a canula connected with a short india-rubber tube has been fastened into a blood-vessel, and has been subsequently filled with an indifferent fluid by means of a pointed glass tubule, the apparatus can be at once put into action; and when it is seen that the injecting fluid begins to be discharged at the pointed extremity of the tube connected with the Woulf's flask, that point is quickly introduced into the india-rubber tube of the canula, and the apparatus is

allowed to work as long as the injection will last. The mercurial apparatus of Hering is well adapted for the expulsion of atmospheric air. If this is not to be obtained, I apply the jet of the waterpipe on the same principle. The atmospheric pressure of the apparatus is measured by means of a manometer, and the rapidity with which the injection is forced onward can be regulated by retarding or accelerating the entrance of the mercury or water.

When the blood-vessels are to be injected, the canula must in all instances be introduced and fastened into the vessel; but, in the case of lymph-vessels, according to Ludwig, the canula need only be stuck into the tissue, and firmly tied to it.

The point of the canula should be cut like a pen, and there should be a groove behind the aperture to prevent the ligature from slipping. In the injection of blood-vessels, all means of escape should be stopped, with the exception of one; and when the fluid flows freely from that, no more fluid should be injected. The injecting fluid distributes itself gradually through all parts, if the pressure be steadily maintained. Even though it is discharged to some extent at one point, injections with solutions of silver should be kept up for at least half an hour, under very gentle pressure; and, in this case, it is not requisite to tie any vessels when the injection is completed. It is only requisite to throw the tissue into dilute alcohol, in order to preserve it perfectly. When it is only required to show the blood-vessels, and not the parietes of the vessels, coloured fluids should be employed; and if the arteries and veins are to be distinguished, each system must be separately injected with a fluid, which must not traverse the capillaries. The material in which the colouring matter is suspended is usually wax, and the colouring substance some granular pigment, as vermilion, red lead, etc. The injection can only be satisfactorily made with a warm syringe and warm tissues, as otherwise it cools too rapidly. After an injection of this kind has been made, the structure of the tissues can no longer be investigated. We can only discern one or more layers formed by the ramification of the vessels, and of course the object can only be examined by direct light. Injections thus made are also used for the so-called corrosion preparations. In the produc-

tion of these, the organ, after being injected, is immersed in some reagent which destroys the tissue, whilst it leaves the injected mass intact. The form of the vascular network is thus obtained in coloured wax, and such preparations can be put up in various ways under glass and in frames. Injections made with transparent solutions are now very common. A canula is inserted into an artery, and the fluid allowed to discharge itself by a vein. The dissolved material penetrates the capillaries whilst the coarsely granular pigment is stopped in the larger vessels. In such preparations it is obvious that no difference can be seen between the arteries and the veins; but, in this condition, they are not fit for microscopic examination. It is still requisite to harden them by freezing mixtures, or by means of alcohol, and then to make fine sections. In these injections it is always requisite that a certain fulness and tension should be given to the vessels; their forms then assume greater definition, and are generally more similar to their natural condition. On this account it is advantageous to dissolve the colouring matter in something which will readily coagulate, and which consequently affords all the advantages of a hardened tissue. Fine gelatine is usually employed, and is dissolved in water over a water bath, the colouring matter already in solution being then added, and the warm mass introduced into a Woulf's bottle, which again must be immersed in a warm water bath. The injection with gelatine is sufficiently tedious if required to be done thoroughly, as the mass stiffens too easily. The organ to be injected should therefore be brought into a warm room, and, where practicable, placed over a water bath which is adjacent to the former one.

The colouring matters usually employed are Prussian blue and carmine; the latter not in a state of complete solution, but partly precipitated by the addition of a little weak acid from its alkaline solution. Thiersch, whose transparent injections are perfect models of this kind of art, uses a transparent green and yellow. He obtains the former from chromate of potash and nitrate of lead, the latter from a mixture of this with blue. When the injection with gelatine is completed, the open vessels must be tied, and the organ introduced or suspended in alcohol contained in a wide-necked bottle, pressure

being carefully avoided. In order to obviate the inconveniences of the method of injecting with warm fluids, Beale recommends a fluid that can be used cold, consisting of colouring matter, water, glycerine, and traces of hydrochloric acid. When the organ has been injected, it is placed in absolute alcohol, and then treated as before. This mode of injection is very convenient, the vessels acquiring a very pretty colour; but they can only be used on organs possessing a certain consistence.

Lastly, the method of self-injection occupies an important position amongst the various modes of injection. It has long been practised in the case of the vascular system of the frog. A pointed glass tube, filled with the coloured injecting fluid, is inserted into the vena cava, and distributed through the system by the force of the heart itself. Kühne and Chrzonszczewsky have thus injected the biliary vessels of living animals by means of colouring matter introduced by the jugular vein. Toldt has very recently practised a similar method for injecting the lymphatics. In the case of the biliary ducts a colouring material (indigo-carmine) in solution is employed, in order that it may be transmitted through the liver cells into the ducts; but in the case of the lymphatics a granular pigment (anilin) precipitated by water from its alcoholic solution, is introduced into the blood. Connected with the introduction of granular pigment is the method of colouring organs through the agency of the food, which has of late years assumed so much importance. This subject will be treated of at length in the first chapter of this work.

CHAPTER I.

THE GENERAL CHARACTERS OF CELLS.

By S. STRICKER.

Independence of Cells.—In the year 1835, Joh. Müller commenced an essay on *Organism and Life*,* with the following words of Kant: "The cause of the particular mode of existence of each part of a living body resides in the whole, while in dead masses each part contains this cause within itself."

From this quotation it is sufficiently evident what rôle was at that time ascribed to the microscopic constituents of the body from the point of view taken by biologists. Fibres, cells, spheroids, and granules were distinguished under the microscope, and it was stated that these structures were not independent so far as their growth was concerned, but were subject to the influence of the vessels. They were on this account differentiated from vegetable tissues, which were supposed to possess an independent existence. A few experiments, however, led to the establishment of certain analogies between vegetable and animal cells. Joh. Müller himself, for example, pointed out the analogy that obtains between the cells of the chorda dorsalis and vegetable cells; and subsequently, when Valentin discovered the nuclei of the cells of the epidermis, he commented upon their similarity to those of the cells of plants.

Henle† made a decided step in advance when he proved that

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* *Physiologie*, Band i., 1835.

† *Symb. ad. Anat. vill. intest.* Berlin, 1837.

the epidermis cells, as they become more superficial, increase in diameter. An instance was thus given of increase without the intermediation of vessels. Schwann* seized the various analogies and points of relation between the cells of animals and plants in a comprehensive and fundamental proposition. Animal cells, he said, are completely analogous to vegetable cells, and are quite as independent in their mode of growth. The vessels of the animal body only cause variations in the distribution of the nutritious fluid.

Joh. Müller† at once and unreservedly adopted this proposition. His observation, that the works of Schwann were the most remarkable that had hitherto appeared in the domain of histology, certainly greatly aided the rapid acceptance they everywhere obtained.

Virchow had already compared the whole organism to a free state, containing individuals endowed with equal privileges if not with equal powers. The views entertained of the physiological significance of the constituents of the tissues, and especially of the animal cells, became, in consequence, completely modified. An impulse leading to the further extension of these ideas resulted from the examination of the lower forms of animal life. Dujardin‡ had discovered in the year 1835 a contractile substance capable of movement in the lower animals, to which he applied the name of sarcode. The singularly interesting phenomena exhibited by the living sarcode has attracted the attention of many observers, as Meyen,§ Huxley, Max Schultze, and Joh. Müller. It was regarded as limited to the lower animals; and though destitute of nerves, the possession of irritability was ascribed to it.‖ Meyen's attempt to show that the Infusoria were unicellular organisms was indeed refuted, but it was admitted that a little mass of sarcode constituted a living and independent being.

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* *Mikroskopische Untersuchungen*, 1839.

† *Jahresbericht*, 1839.

‡ *Annal. des Sci. Nat.*, Tom. vii.

§ See the general literature of this subject in E. Häckel, *Die Radiolarien*, 1862.

‖ See Max Schultze's *Organism d. Polythalamien*, 1854.

The discovery of Siebold,* that the vitelline spheres of the egg of the Planariæ exhibit alternate contractions and dilatations, which, under favourable conditions, continue for hours, and the various subsequent discoveries of similar movements, or changes of form occurring in the colourless blood corpuscles, in pigment cells, and elsewhere, have led Kölliker† to express the opinion that the contents of all cells are contractile.

Virchow‡ gave a still more precise expression of opinion when he stated that ciliary movement is to be attributed to a contractile substance; to which conclusion he was drawn by the discovery that under certain circumstances these movements, after having ceased, could again be excited by dilute solutions of the fixed alkalies.

Leydig§ referred to the significance of the movements occurring in the spherules of the yolk, which he, in common with Ecker, regarded as evident phenomena of life.

Kühne‖ undertook a series of comparative physiological and chemical researches on muscular substance and sarcode, and pointed out the similarity of the phenomena they presented in the act of dying.

By all of these, however, the sarcodal substance was regarded as something different from animalcules, and as a material *sui generis*.

Max Schultze¶ was the first to show that sarcode is analogous to the body or contents of animal cells, and that on this account the infusorial animalcules possessed of independent life were simple or compound (fused *inter se*) cells. Schwann's views received support from these statements. According to the new doctrine, the cell was the typical form element of nearly the whole organic kingdom. The previous inquiries on the contractile sarcode could now be applied to the knowledge of the animal cell, and the renewed parallel

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* *Froriep. Notizen*, No. 380, p. 85.
† *Würzburg. Verhand.*, Band viii.
‡ Virchow's *Archiv*, Band v.
§ *Handbuch der Histologie*, 1856.
‖ Müller's *Archiv*, 1859, p. 817.
¶ Müller's *Archiv*, 1861, p. 17.

investigations between sarcode and the protoplasm of the plant on the one hand, and of animal cells on the other, undertaken by E. Brücke,* E. Häckel,† Max Schultze,‡ and W. Kühne,§ have, in a very short space of time, advanced our knowledge on these points to a greater extent than the investigations of the preceding twenty years.

Brücke, who regards the cells as elementary organisms, admirably expresses the ideas, the development of which has been lightly sketched in the following passage:—

"If we consider," he says, "how complicated the mechanical arrangements must be which lie at the root of the spontaneous movements of cells, and if we consider further that up to the present time we have only paid attention with the microscope to obvious and perceptible movements, and that no regard has been paid to the arrangements, by virtue of which the little organism nourishes itself, increases in size, and begets its like, nor any to those means by which it displays its specific attributes; if we, I say, consider all this, we must necessarily recognise that we have to deal here with an organism, the complication of which, although, truly, not comparable with that of an animal, nor affording any good reason for believing that it is itself composed of innumerable small organisms, yet constitutes one to which we may fairly attribute the possession of a highly artificial structure, the essential architectural elements of which are, however, completely beyond our grasp."

Ideal Type of a Cell.—Johann Müller proved that the cells of the chorda dorsalis possessed proper walls. In similar cells from the frog, Schwann demonstrated the existence of a nucleus, and was by this discovery first led to perceive the analogy between the cells of animals and plants. Here, then, we have a cavity bounded by walls, in the interior of which is a nucleus.

Scarcely any structure is to be met with in the whole range

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* *Elementar-organismen, Wiener Sitzungsberichte*, 1861.

† *Loc. cit.*

‡ *Protoplasm der Rhizopoden.* Leipzig, 1863.

§ *Protoplasma und die Contractilität.* Leipzig, 1864.

of animal tissues which is more suggestive of comparison with that which the botanists call a cell. (See p. 6.)

All animal cells were at this time considered to be constructed on the same principle, being held to possess a cell wall, enclosing a cavity, in which were fluid contents and a nucleus; when the membrane was not visible, it was either supposed to have burst, or was admitted to be present. In the cells of the egg a membrane was recognised by Krause,* from the presence of a double contour line. This mode of proof was not, however, strongly supported. C. H. Schultz considered he was able to exhibit the membrane of the blood corpuscles by the action of water upon them, inasmuch as they swelled up in this fluid, and assumed a spherical form; he also believed the nucleus revolved in the interior of the sphere.

The corpuscles of pus and of mucus had, however, even in the eyes of Schwann no distinctly demonstrable membrane; he regarded them as minute roundish masses, containing a nucleus, which might be termed cells, because this was the elementary form of all animal and vegetable cells.

In accordance with the general views of Schwann, respecting the analogy of animal and vegetable cells, the ideal type of a cell was constructed.

Individual and scattered opposition to this ideal type of a cell was ineffectual so long as the whole theory of Schwann was contested, as it was, for example, by Arnold.†

With sure footing, and still resting on Schwann's conclusions, Leydig also abandoned the scheme of cell construction already mentioned.‡ He maintained that the contents of the cell are of higher dignity than the membrane, and constitute the material basis for the sensible and irritable processes; and that the conception of a cell requires the presence of only a little mass of substance, inclosing a nucleus. The cell membrane is, in his view, only the hardened external layer of the cell substance.

Max Schultze was, however, the first who effectually directed

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* Müller's *Archiv*, 1837, p. 139.

† See his *Anatomie*, 1845, Band i., p. 144.

‡ *Loc. cit.*

the views of histologists away from the idea of the vesicular construction of cells. As has already been stated, Max Schultze had himself furnished a new definition of a cell, which constituted an extension of the theory of Schwann. Max Schultze also defined the cell to be a little clump of matter (protoplasm), with a nucleus. The importance of this definition, however, did not lie in the fact that the existence of a membrane in many cells was denied—that had been already more or less positively stated before Max Schultze. The essential point was, that the identity of the so-called cell contents with the primary animal substance, or sarcode, was clearly recognised.

Little advance had, indeed, been made in the way of establishing a basis of life; for nothing more was known of the processes which take place in the living substance, than of those that were carried on in vesicles—perhaps still less—for all the phenomena of diffusion were intelligible on the vesicular theory, whilst it was difficult now to account for them. Naturalists, however, were familiar with irritable independently existing animals, but not with the idea of an irritable and independent vesicle obtaining its food by the laws of diffusion. The conception of a living cell body, or elementary organism (Brücke), has been an exceedingly satisfactory one to biologists, on the same principle that it gives us a great degree of satisfaction to be able to attribute to some familiar circumstance a noise in our sleeping apartment, on the origin of which we have long speculated in vain.

Those membranes of the animal cell which did not exhibit a double contour, were compared by intelligent histologists, not with the cellulose investment, but with the primordial utricle of the cells of plants. Botanists* distinguish a cellulose investment in the cells of plants, within which is the protoplasm that includes the nucleus and the solid and fluid contents of the cell. The protoplasmic mass externally, where it comes into contact with the wall of cellulose, was supposed to be invested by a very thin membrane—the primordial utricle. But Pringsheim† has shown that such a primordial utricle does not exist, the

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* H. v. Mohl, *Vermischte Schriften, Botan. Inhalts*, 1845.

† *Bau und Bildung d. Pflanzenzellen*, 1854.

protoplasm lying in apposition with the inner surface of the cell wall. The term protoplasm had already been brought into use by Remak for the contents of animal cells. Max Schultze proposed to apply the term to the living mass of the cell, and since then the word protoplasm has been very generally employed.

Max Schultze* takes the embryonal cell as the basis and starting-point of his definition. "The most important cells," he remarks, "those in which the fulness of cell life, the unlimited power of tissue formation, is most distinctly evident, are clearly the embryonal cells, which proceed from the division of the cells of the ovum. We may see in these the true archetype of a cell, and yet they only consist of a little mass of protoplasm and a nucleus. Both the nucleus and the protoplasm are products of the division of similar constituents of another cell. Such cells include a living force in their interior, essentially possessed by the protoplasm, although it is true that the nucleus likewise plays an important part, not hitherto known with sufficient accuracy. The protoplasm is no farther isolated from external objects than by the circumstance that it will not combine with the surrounding medium, and that it constitutes, with the nucleus, a single whole. A distinct membrane may, indeed, appear on the surface formed by the conversion of the outer layer of the protoplasm, but then it must be allowed to be an early indication of a retrograde process. A cell invested by such a membrane can no longer divide—that is a power possessed by the enclosed protoplasm alone. A cell with a membrane differentiated in its chemical characters from the enclosed protoplasm, is like an encysted infusorial animalcule."

Brücke† goes a step farther in his definition of a cell, maintaining that no proof has been given that the nucleus is indispensable to our conception of it. He rests his statement essentially on the fact that cells are known to occur in the cryptogamia in which no nucleus is visible. "We have," he says, "no positive information, either respecting the origin or the function of the nucleus; even the constancy of

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* *Loc. cit.*, p. 8.

† *Die Elementar-organismen*, pp. 18—22.

its occurrence appears to be subject to certain limitations, especially if we consider the cells of cryptogams, and do not start with the presupposition that, even in those cases where no nucleus is visible, it must nevertheless be present." The opinion of Brücke undoubtedly gains in weight, the more carefully the subject is considered.

Max Schultze* has discovered a non-nucleated Amœba (*Amœba porrecta*) in the Adriatic; E. Häckel† a larger non-nucleated Protista (*Protogenes primordialis*) in the Mediterranean; and lastly, Cienkowski‡ has described two non-nucleated monads, namely, Monas amyli and Protomonas amyli. Häckel states, in reference to his protista, that it propagates by division.

It is, moreover, a fact, first made known by V. Baer, that the germinal vesicle of the impregnated egg—that is, the nucleus of the ovum—vanishes, and that the further process of development commences with a new generation of nuclei. I must express, in regard to the egg of the frog, my entire concurrence with V. Baer in regard to the question at issue. I have undertaken a great number of comparative investigations between fertilised and unfertilised ova in the same mode as that employed by him, and have found a germinal vesicle in the latter as a rule, whilst in the former there is only a cavity left, or even a total absence of any trace of its existence. But the ova of the more highly organised animals pass, as is well known, through various stages or grades of development till they reach a state in which their life terminates, and these ascending stages of development may, without straining the point, be generally compared with the ascending grades of organisation which characterise the existing world. It is therefore but a step to admit that the commencing stages of the process of development correspond to the lowest forms of animal life. The existence of the non-nucleated cryptogams and of the non-nucleated protista which are now known, speak strongly in favour of such an analogy.

But if we desire to be logical, if we do not desire to advance the statement that the non-nucleated bodies of the lower plants

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* *Organism der Polythalamien*, 1854.

† *Zeitschrift für wiss. Zool.*, 1865, Band xv.

‡ Max Schultze's *Archiv*, 1865.

and animals and the fertilised ovum occupy an unique and isolated position which is not assumed by any other being in the whole scale of creation, we must exclude the nucleus as an unnecessary factor in the ideal type of an elementary organism. We must also in future apply the histological term cell to the morphological elements of the higher animals or to independent living organisms, even if we are unable to discover anything more in their structure than that they are little masses of animal sarcode or protoplasm. Nor will any essential change be made in our views even if it be hereafter proved that there are cases where the nucleus is not only present but plays an extraordinarily important rôle.

I* have shown that little masses of protoplasm, destitute of nuclei, and which might be presumed to be the remains of cells, may still present some of the phenomena of life. I also now know that in other places where many young cells are collected together, fragments or minute separated particles occur about the size of a nucleolus, which, if they become attached to the slide, sometimes exhibit very lively movements, and this especially if the object plate be warmed to from 68° to 70° Fahr.

May we now, in consequence of our new definition, consider these little masses as cells? and shall we be justified in giving this name to all the minute particles which, when armed with instruments of still greater penetration, we may be able to perceive and find capable of spontaneous movements? In the present state of our knowledge we shall certainly reply in the negative. We shall continue to regard such minute masses as living or organised matter without reference to their size, so long as the optical means of research at our disposal do not permit us to make the observations necessary for a different statement.

We cannot, however, term these masses cells, any more than we can apply the name of the whole animal to the excised heart of a tortoise. In order that we should apply the term "cell" to such an isolated fragment of living substance, it is necessary that we should recognise the whole group of phe-

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* *Uber contractile Korper in der Milch,* "On the contractile bodies in Milk," *Wiener Sitzungsberichte,* 1866.

nomena which are characteristic of an independent animal—an independent organism.

PHYSIOLOGICAL PECULIARITIES OF CELLS.—Contractile substance, or protoplasm, appears, when examined with the best microscopes, to be homogeneous, or destitute of structure. It rarely occurs, however, in a pure state; for small particles are usually imbedded in it, which have either been taken up from without, or have formed in the interior as a consequence of chemical processes. If the protoplasm contain many coloured corpuscles, the cell is termed a pigment cell; if it contain fat molecules, a fat or granule cell. The presence of small colourless, dull, or shining granules is indicated by the term granular applied to the cell, and of such cells two kinds are distinguished—those that are coarsely and those that are finely granular.

When other kinds of material are contained in the cell, their presence is indicated by appropriate terms. It is thus usual to speak of starch-holding cells, and the like.

Since the researches of Häckel (see p. 16) have shown us that foreign matters can penetrate into the interior of the protoplasm, the origin of all such particles must be investigated. We must determine in every case whether a body which lies in the interior of the cell is the result of some chemical process in the interior of the protoplasm, or has been introduced from without. If particles of colouring matter are artificially caused to enter, as has been successfully accomplished by Recklinghausen, Max Schultze, Billroth, Cohnheim, and others; then the question as to whence the colouring matter proceeds is answered by the experiment itself. But it is more difficult to decide from whence those bodies that are found imbedded in cells proceed, which occur without the agency of the experimenter. The determination of this point may prove, however, of extraordinary importance. Since, for example, Preyer showed that portions of red corpuscles are eaten by the amœboid cells of the frog, we could not admit without much proof that the presence of red corpuscles in the interior of the white was due to the development of the former in the interior of the latter.

The consistence of protoplasm varies within moderately wide limits. It may, like a fluid, form drops, assuming, when in small quantities, a spherical form, or may extend itself upon

the slide like a gelatinous body; or, lastly, it may contract up into a resistant ball.

Protoplasm may therefore be said to be fluid, or solid, or gelatinous. Its states of aggregation are subject to constant change, and none of the ordinary terms employed for this purpose will be in all cases accurate.

Protoplasm is termed a living substance, and the application of this term is based upon its exhibiting the sum of those phenomena which we have learned by experience to be characteristic of living animals. These phenomena are active or spontaneous movement, nutrition and growth, and the capability of reproducing its like.

The movement of cells is easily to be seen. The changes of which it is the result take place in so short a space of time that they may be followed with the eye. The growth of the cells is a process of a slower nature, and cannot be directly observed; nor has any one, as yet, been able to place the cells under the microscope, under such favourable conditions as to witness their increase in size. We must therefore be led by analogy to the conclusion that this really takes place.

Various observations have been directly made on the nutrition of unicellular animals. It may be seen how they take up foreign bodies, and nutritious material, into their bodies, and some of the changes of the material introduced may be followed. It is difficult to observe the mode of nutrition that occurs in the cells of the compound animal body, because the nutritive materials are brought to them in the form of solution in the juices of the animal body. Moreover, the processes by which the dissolved substances penetrate the cells is concealed from our observation.

The act of reproduction depends on two separate processes; first, on the growth of the mother-cell, and secondly, on the detachment of the daughter-cell (birth). The latter alone is subject to direct observation, and usually this only is understood when reproduction is under consideration.

PHENOMENA OF MOVEMENT IN CELLS.—We conclude that movement occurs in cells, either from certain movements of the

granules that are imbedded in the protoplasm, or from the occurrence of certain changes in the form of the protoplasm itself. The movement of the granules in this case is a passive movement. The granules which have been introduced from without, as well as those which have developed in the interior, providing they are not too heavy, move as the result of the action of the forces we are about to consider.

The movement of the granules is either continuous or vibratory.

The continuous movement, again, presents two forms; first, a relatively slow progression, corresponding to and following the changes of form of the cell.

Engelmann* states particularly he has observed, in the corpuscles of the cornea, that they begin to move in order, from before, backwards, and refers to similar observations of Hofmeister on the Plasmodia of the Myxomycetæ.

Secondly, There is a swifter flowing movement that far exceeds the changes of form of the protoplasm in rapidity.

Max Schultze describes the movement of the granules in the threads of sarcode that the Foraminifera project through the apertures of the shell, as a gliding or streaming motion of granules imbedded in a sarcodal substance.† "As the passengers in a broad street swarm together, so do the granules in one of the broader threads make their way by one another, oftentimes stopping and hesitating, yet always pursuing a determinate direction, corresponding to the long axis of the thread. They frequently become stationary in the middle of their course, and then turn round; but the greater number pass to the extreme end of the thread, and then reverse the direction of their movement." It cannot be doubted that these continuous motions depend on vital processes in the cells. At all events, we are acquainted with no analogous phenomena in unorganised bodies.

The vibratory movement of the granules calls to mind the so-called molecular movement of Brown. It may be witnessed in the salivary corpuscles, and under certain conditions in the

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* *Ueber die Hornhaut.* Leipzig, 1867.

† *Das Protoplasm d. Rhizopoden*, p. 11.

colourless blood corpuscles, pus corpuscles, and others. On this account it has been doubted whether these movements really depend on the vital properties of the protoplasm. Such movements, it may be observed, occur also in dead cells, as in the case of granules that have escaped from cells undergoing disintegration, which continue to move, provided that the medium they enter does not present any obstacle.

Similar movements, too, are found in cells that are clearly living. The dancing movement ceases in the interior of the corpuscles of saliva on the cautious addition of a solution of common salt, containing from $\frac{1}{2}$ to 1 per cent.; but this still permits the movements of fresh pus or lymph corpuscles to continue.

Recklinghausen* has described similar phenomena in the latter kind of corpuscles. When the menstruum is diluted with water, they become spherical (an experiment that had already been performed by H. Müller and Reinhardt),† and the granules in their interior begin to dance; but as soon as the fluid becomes somewhat more concentrated in consequence of evaporation from the margins of the cover, this vibratory movement ceases, and the corpuscles commence again to undergo their customary changes in form.

We see here, then, clearly enough, that two phenomena alternate: if the corpuscles are spherical, the granules dance in their interior; but if the corpuscles undergo changes of form, then the granules cease to vibrate. It is rare to see the so-called molecular movements in cells which change their shape. It may, however, be occasionally observed in the colourless blood corpuscles of the newt, after the addition of water. The question whether the vibratory movement of the granules stands in relation to the life of the protoplasm is only applicable to such living cells.

Brücke‡ has referred to the possibility of this connection, in consideration of the circumstance that the movements are arrested by induction currents of sufficient intensity.

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* Virchow's *Archiv*, Band xxviii.

† Virchow's *Archiv*, Band. i.

‡ *Ueber die sogenannte Molecularen*, "On the so-called Molecules," *Wiener Sitzungsberichte*, 1862.

Böttcher,* on the other hand, has expressed his doubt upon the existence of any such connection, on the ground that the granules which vibrate in the cells continue the same movement when they have escaped from the interior (by bursting of the cells), provided that the medium into which they pass is of an appropriate nature.

Neumann† founded his objection on the fact that the vibratile movement still occurred in cells which were dead or on the point of death.

The idea of a connection existing between the movement and the life of the protoplasm is essentially based upon these facts; first, that the cells in which it occurs are living cells, and secondly, that changes in the phenomena of life induce, or are followed by, changes in the motion of the granules. In the meantime, observation of the movement of the granules alone cannot enable us to draw any conclusion in regard to its dependance on life, so long as it is only a vibratory and not a progressive movement, and so long as some peculiarities are not discovered in these vibratory movements, which justify such a conclusion.

a. CHANGES IN FORM of the entire mass of the protoplasmic mass are most strongly marked in the lower forms of animal life.

Max Schultze,‡ in his description of the mode in which the Amœba of Ehrenberg or Proteus (O. F. Müller) obtains its food, furnishes the following lively picture of its movements :—

When an amœba approximates another animal whose movements are not so swift as to enable it to escape from its enemy, it embraces it with its many-stalked body. The processes meeting on either side, coalesce, and after thus investing the whole mass with animal substance, the Amœba maintains its grasp till it has abstracted all the portions that are soluble. On account of this remarkable peculiarity of the Amœba, those cells which possess the power of spontaneously moving, are termed amœboid cells. It is rare, however, for the cells of the more highly organised animals to move so rapidly as the Amœba itself.

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* Virchow's *Archiv*, Band xxxv.

† Reichert and Du Bois Reymond's *Archiv*, 1867.

‡ *Polythalamien*, 1854, p. 8.

Their movements are either limited to gradual change of form, or to the protrusion of processes which either drag the rest of the body after them, or are again withdrawn. The processes may assume the form of threads, swellings, tuberous elevations, or broad flattened projections or tufts, and may present the greatest diversities of form.

If the alterations in shape are desired to be accurately noted, the cell must be placed upon a slide, or on a piece of tissue, or may even be attached to the cover; for if the cells swim in fluid, it is possible they may turn, and thus present different surfaces to the observer. No conclusion can be drawn respecting the life of a cell, from the observation of a single change of form, since it is impossible to ascertain whether some unknown physical influence may not have wrought the change. Those alterations of form only which may be perceived in the object when the field of view is stationary, and when the object is adherent to the slide, and which are frequently repeated, enable us to determine the presence of life in it.

Conversely also, we must not consider a quiescent protoplasmic mass as necessarily dead, even if we are unable artificially to excite movement by means of reagents. The protoplasmic substance may possibly be encapsuled when it is not in a state to change its form, and even if it be naked, some unknown cause may hinder its movements. Hence, it cannot be said that the salivary corpuscles are dead, because as a rule they do not change their external form.

Protoplasmic corpuscles are not only able to change their form, but their place also; they can wander. This is accomplished by the protrusion of one portion of their mass, which drags the rest after it. If such alterations of form are repeated several times, and in the same direction, locomotion is effected.

It must not be overlooked that entire cells may exhibit vibratory movements in fluids obviously subject to the laws of the Brunonian molecular movements. The stellate blood corpuscles of mammals, for example, do so as a rule. Such vibratory movements are to be clearly distinguished from the migrations of cells. Cells can only move from place to place when resting on a firm basis. They may swim in fluids, owing

to the agency of currents, but not through their own active movements.

The capability of moving from one place to another, possessed by the Amœba, has long been known. The migratory power of the Foraminifera, by means of the processes of their structureless substance protruded through the openings of their shell, has also been frequently observed. But Recklinghausen* was the first to notice that the cells in complex animal bodies can also perform movements of locomotion, and by his observation introduced a fact to our knowledge having a very wide and important bearing.

E. Häckel, whilst injecting Thetis fimbria with indigo, discovered that fine particles of colouring matter could penetrate into the interior of the blood corpuscles. The artificial introduction of colouring matters into cells is now termed giving them a supply of food. If, into the medium in which the cells are suspended (for example, blood plasma), a finely granular colouring matter be introduced, some of the particles of the latter are soon found to cleave to the surface of the cells, and to pass from thence into their interior.

By the aid of this mode of supplying food, Recklinghausen has furnished the important proof that pus corpuscles are not always generated where they are found. He has shown that pus corpuscles can migrate into the meshes even of a dead cornea, and has by this observation opened up a new path for every department of pathological inquiry. These also are matters of fact that exert no little influence on physiology generally. I† have myself shown that in the construction of the body of the embryo, the movement of masses of cells to form the rudiments of organs, depends on the migration of the embryonal cells within the ovum. Cohnheim‡ has also very recently, by demonstrating that the colourless corpuscles can leave the vessels, and migrate, and that there may be a transplantation of living cells from one organ into another, and from one region of the body to another, furnished us with in-

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* Virchow's *Archiv*, Band xxviii.

† *Wiener Sitzungsberichte*, 1864.

‡ Virchow's *Archiv*, Band xi.

formation, the importance of which cannot at present be estimated.

Hering* has endeavoured to explain the passage both of coloured and of colourless blood corpuscles through the walls of the vascular system, by comparing it with the filtration of colloidal substances. But in whatever way the process may be explained, the fact remains that the white corpuscles leave the interior of the vascular system, and are thus enabled to traverse various regions of the body.

In stating that protoplasm is capable of active or vital movements, we have by no means admitted the existence of an immaterial force. Ed. Weber † has expressed himself very decidedly upon this point, and at the present day the position he took up is still tenable. "According to my view," said Weber, "the movements of any living body are not dependent upon two kinds of force—namely, first upon forces which are exerted on this body by other bodies, and secondly upon forces which are exerted on this body by life; but there is only one kind of force on which the movements of all bodies depend—namely, the force which is exerted on it by other bodies." We name the movements of certain bodies "vital," in the sense that the forces which we then call into play are subject to certain other varying influences, and we denominate the apparatus and the processes of which these influences are the result, "organization" and "life."

It is customary also to call the vital movements of protoplasm spontaneous. But this only shows that we are ignorant of the forces by which the movements are originated and sustained. We no longer term the movement of striated muscle spontaneous, because we know the external influences or stimuli through which it can be excited. And so also there can be no doubt that as soon as we have acquired a knowledge of all the external influences by which movements in protoplasm can be induced, we shall cease to term them spontaneous. Thus, in an analogous case, we say the production of heat by coal is immediately dependent on our placing it on the fire, *i.e.* on raising its temperature. Here the process of heating is the external influence or stimulus which induces a change in the molecular structure; and as a consequence of this molecular change, active force is set free, which becomes perceptible to us in the form of heat. The production

* *Wiener Sitzungsberichte*, 1868.

† Müller's *Archiv*, 1858.

of heat by carbon is an independent power, dependent on the very nature of its substance, but it is by no means a spontaneous power. The analogy, however, has only a one-sided value, since, if the coal is once burnt, it can generate no new active force; but the contractile substance is capable of restitution.

The movements of contractile substances may be altered, accelerated, retarded, or altogether stopped, by external influences (stimuli), which may vary greatly in kind and degree.

Amongst the known conditions that exert an influence on the movements of protoplasm, we may enumerate the variation of temperature. The oldest reference to this fact was made by Weber,* when he said the movement of cilia could be accelerated by warmth. Kühne† also remarked that the motions of amœbæ could be arrested by iced water, but that on raising the temperature they recommenced.

Since Max Schultze‡ has made the warming of the slide an important assistance in micro-physiological investigations, we have learnt that the locomotive cells of warm-blooded animals can maintain their movements for a long time, external to the organism, if kept at the ordinary temperature of the animal from which they have been taken. We are unable, however, to give any precise statements possessing general application, respecting the influence of temperature.

Still, as a general rule, an exaltation of a few degrees above the temperature at which the organisms customarily live, accelerates their movements, whilst a corresponding depression retards them. If the temperature exceed certain limits, however, their life is imperilled. The eggs of trout, for instance, undergo segmentation capitally in iced water, but in a warm room soon die.

The influence of temperature on the movement of cells is a point of particular interest in reference to their migration. Max Schultze§ has demonstrated that the colourless corpuscles

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* Canstatt's *Jahresbericht*, 1847, p. 59.

† *Das Protoplasm.* Leipzig, 1864.

‡ Schultze's *Archiv*, Band i.

§ *Loc. cit.*

of human blood are capable of effecting a considerable amount of locomotion at a temperature of from 100° Fahr. to 104° Fahr. It is well known how great is the influence of particular temperatures on the development of the egg, and even if the movement of the cells is not the chief factor in this process, it certainly plays a very important part in it. We may readily conceive that an analogous influence must be exerted by any increase of temperature occurring in pathological processes.

A peculiar effect of temperature is described by Kühne,* as observable in the fresh-water amœba, which at 95° Fahr. assumes a spherical form.

Lastly, Peremeschko † states that the large cells at the bottom of the yolk cavity in the eggs of fowls, contract and dilate at a temperature of from 89·3° Fahr. to 93° Fahr.

b. Mechanical Influences.—Kühne was the first to comment on the effects of indirect mechanical irritation, stating that after he had stimulated the margin of the cornea in a frog, he saw stellate corpuscles become fusiform.

I‡ have made a few experiments on the effects of direct mechanical irritation, and have observed that when blood diluted with a solution of common salt, containing one half per cent., is placed under a cover, and this last, by the withdrawal of the fluid, is allowed to sink to such an extent that the white corpuscles are flattened out, they alter their shape with considerable vivacity, especially if they are allowed to remain in this position for some time. If now a drop of fluid is brought to the margin of the cover, this will again be raised from the slide in proportion to the quantity added. The flat corpuscles may now be observed to contract into small angular lumps, and after a short time to change from this into a moderately expanded form.

The compressed corpuscles here behave like the muscles of insects under the compressorium, which continue their movements for a time,

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* *Protoplasma*, 1864.

† *Wiener Sitzungsberichte*, 1868.

‡ *Wiener Sitzungsberichte*, 1867.

even when the pressure upon them prevents any increase in thickness. It is evident from this experiment that protoplasm is an elastic body, since it contracts when the extending force is removed. The contraction, however, appears to correspond here with the elasticity of the irritated substance, because a shortening occurs which is not maintained. An additional argument in favour of this view is, that the experiment is more successful when it is tried a second or third time. The corpuscles then contract much more energetically than at first.

c. Electrical Stimuli.—The action of electric currents on protoplasm is very variable.

The excitation of amœboid movements by means of weak induction currents has, up to the present time, only been observed by Kühne in amœbæ, and by Golubew in certain white corpuscles of the blood of the frog.

Kühne* saw amœbæ assume a spheroidal form, when made to form part of a constant current; whilst, after exposure to an intermittent current, the stellate corpuscles of the cornea became fusiform, and then reassumed their original shape.

Golubew† states, from experiments made in Rollett's laboratory, that after being repeatedly irritated the cells become flattened, but even in that state exhibit changes of form. If stronger stimuli are applied to them in this condition, the disc-like mass again contracts and becomes spheroidal. He further observes that the fusiform colourless cells of the blood of the frog, which present no spontaneous movements, when moderately irritated, contract to spheroidal masses, but soon again revert to their original shape. I‡ have observed contractions and dilatations to take place in embryonal capillary vessels after the action of induction currents.

Kühne§ has observed the following law of contraction in the protoplasm of Actinophrys eichhornii during the action of a constant current:—

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* *Loc. cit.*

† *Wiener Sitzungsberichte*, 1868.

‡ *Wiener Sitzungsberichte*, 1866.

§ *Loc. cit.*

	Positive pole, or electrode entrance of current.	Negative pole, or electrode exit of current.
Closure - - - -	Contraction - - -	0
Current passing - - -	Tetanus - - -	0
Opening - - - - -	0 - - -	Contraction.

After being exposed to the action of moderately strong induction currents, protoplasm assumes a spheroidal form. This observation was first made by Kühne in the amœba, and has since been corroborated by Neumann, in regard to the colourless corpuscles of human blood, and by Golubew in those of the frog. Kühne states that amœbæ which have become spherical from the action of induction currents, after a short time recommence their ordinary movements. Golubew makes the same remark, but observes that the movements of the colourless corpuscles of the frog are of a more undulatory character, though they send out, as usual, pointed processes.

According to Neumann and Golubew, when strongly irritated, the granules in the spherical cells exhibit vibratory or so-called molecular movements.

Brücke* saw salivary corpuscles burst under the influence of strong induction currents. Kühne witnessed a similar phenomenon in an amœba.

Kühne describes the spheroidal condition of the amœba, produced by stimuli, as a kind of tetanus, and considers that, in the state of maximum contraction, these animals assume a spherical form.

Hermann, however, suggests an essentially different explanation. It is possible, he remarks, that the excitation diminishes certain resisting forces which have previously prevented the cell from assuming a spherical form. The spherical form therefore, he thinks, may correspond either to the state of rest, or to the state of tetanus.

Kistiakowsky† has observed an acceleration of ciliary movement to be produced by the constant current.

Engelmann‡ gives the following series of laws of this action:—

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* *Ueber die sogenannte Molecular-bewegung*, *loc. cit.*

† *Wiener Sitzungsberichte*, 1865.

‡ *Centralblatt*, 1868.

(*a*) Every variation in the intensity of the current, whether positive or negative, providing it be sudden, acts as an excitant.

(*b*) A single variation in the intensity of the current induces a series of alternate contractions and relaxations.

(*c*) A single excitation induces changes which may be divided into three stages: That of latent excitation (which with opening-induction shocks is scarcely perceptible, and is hence generally longer the weaker the shock); secondly, the stage of increasing energy (which also lasts longer in proportion to the feebleness of the shock); and, lastly, the stage of diminishing energy (which is so much the more rapid the weaker the shock).

(*d*) The closure of a constant current is a stronger stimulus than its opening.

(*e*) The direction in which the current traverses ciliated cells appears to have no influence on the amount of irritation exerted.

(*f*) The movement may be retarded by the application of a very strong electrical current, or may even be altogether stopped, the cell at the same time being destroyed. The same thing occurs on producing long-continued tetanisation with strong alternate currents.

d. Nervous Excitation.—On this point only a single direct observation by Kühne can be adduced; namely, that the contraction of certain stellate cells in the cornea of the frog may be induced by excitation of the corneal nerves. Brücke* had long before furnished evidence in regard to this by referring to the very well-marked phenomena of contraction that are visible in the pigment cells of the skin of the chameleon, and which can readily be excited reflectorially by irritation of the sensory nerves.

e. Chemical Stimuli.—Amongst these we may first mention the influence of water. Amœboid movements can be excited in the segmentation spheres of the egg of the frog by

* *Denkschriften die Wiener Akad.*, Band iv., p. 203.

the addition of water: hyaline processes are thrust out, in the interior of which a streaming motion of granules can be discerned, so that the form of the cell undergoes a change. At other times the processes are again withdrawn, or undergo repeated alterations of form after they have remained protruded for a short period. Ecker* regarded these phenomena as indications of spontaneous movement, but I† have shown that the movements of these cells, when no water has been added, are of quite a different kind, and that the above occur only on the addition of that fluid.

The streaming movements of the granules contained in the pseudopodia of the marine rhizopods is also arrested by distilled water.‡ The greater number of amœboid cells become globular when exposed to the action of water, but after a few seconds a vibratory movement of the granules is observable, after which the cells generally burst; some, however, remain globular for a time, and then recommence their amœboid movements: this is particularly the case if, as has already been mentioned, they are moistened with a one-half per cent. solution of common salt.

The cells that assume a globular form on the addition of water, seem also to increase in size, from which it may be concluded that they imbibe some of the fluid.

The laws by which water or a solution of any substance is thus taken up are unknown. It seems probable, however, that diffusion plays a part in the process.

We may also conceive that the water which has penetrated into the interior of the contractile substances acts as a stimulus, because we are already acquainted with the similar action exerted by water on muscular tissue, and because electrical currents produce similar effects on the cells.

The statement made by Hermann, that the spherical condition assumed by the cells in water or other dilute medium is a state of rest, is certainly plausible. The circumstance that they will remain

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* *Icones Physiol.*

† *Ueber die Selbstandige Bewegung, Wiener Sitzungsberichte*, 1864.

‡ Max Schultze's *Archiv*, Band ii.

spherical for hours, without losing their vital properties, as may be seen in the case of the salivary corpuscles, is also in favour of it.

The coalescence of the spherical cells described by Brücke, Neumann, and Golubew, can then be very naturally explained; for it may be said that, as a consequence of the stimulus, the opposing influences are diminished, and the protoplasm now follows the laws of ordinary liquids—it forms drops, and these coalesce. The act of bursting in water must, then, be regarded as due to a suddenly produced partial coagulation resulting from the more energetic action of the fluid.

If to the medium in which the spherical cells are contained a one-half per cent. solution of common salt is gradually added, the protoplasm resumes its apparent activity, and recommences the usual changes of form. But if the solution added be concentrated, the cells shrink up. It has not been, as yet, accurately ascertained what strength of solution is compatible with the life of the cells, nor for what length of time the action may be continued. The proportion of water in many protoplasmic substances may undergo great variations without destruction of life. The myxomycetæ can even be completely dried up, and yet when again moistened may continue to live.

Max Schultze and Kühne have observed similar results to those above described, to result from the action of water after the addition of very dilute acids and alkalies.

An elegant experiment has been made by Kühne,* showing the influence of gases on the movements of protoplasm. He has pointed out that the ciliated cells of the gills of Anodonta cease to lash in hydrogen and in carbonic acid, but that it is only requisite to admit atmospheric air in order to effect the re-establishment of the movements. This experiment shows that carbonic acid acts injuriously like other acids.

Weak alkaline reaction in the fluid in which the cells are contained, is favourable to their movements, but acids tend to arrest them.

The contractility of the protoplasm is of the greatest importance to the entire organism to which it belongs, for ciliary movement depends upon it.

* Max Schultze's *Archiv*, Band ii.

As we now know from the researches of Schweigger-Seidel and La Valette, that the spermatozoids are not essentially nuclear structures, but are also composed of protoplasm, their movements must likewise be attributed to this substance.

Cell division and germination are likewise consequences of its contractility.

Lastly, also the migrations of cells are dependent upon it, of the importance of which to the organism at large we have already spoken.

Hermann has made an attempt to explain the phenomena of movement. The protrusion of a process, he says, can only be regarded in the light of a partial contraction, which, whilst it occurs in the direction of a striving on the part of the cell (or, better, of a striving surface), drives the superjacent segment before it. If, then, renewed contraction continually occur, it must always become thinner and more thread-like. Hermann makes no remark, however, on the retraction of the processes. But if Hermann's theory were adopted, there would not be much difficulty in explaining this by admitting contractions in other directions.

Metamorphosis of Tissue.—Only a single direct observation by Kühne* exists in regard to the metamorphosis of tissue that takes place in the living cell. According to his researches, ciliary movement is connected with the consumption of oxygen, and there can be no doubt that the cells are capable of withdrawing oxygen from loose chemical combination. Ciliary movement continues in an atmosphere of hydrogen, and in a solution of oxygenated hœmoglobin, till all the loosely combined oxygen of the latter, as may be proved by spectrum analysis, is consumed. Moreover, from indirect experiments, we are justified in admitting a metamorphosis of tissue in the cells, and are hence in a position to realize the more accurate data which have been acquired respecting the metamorphosis of tissue in animals. The results which have been arrived at from investigation on muscles are particularly important. Muscular fibres are metamorphosed cells, and they consist essentially of contractile substances, the internal structure of which differs

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* Max Schultze's *Archiv*, Band ii.

entirely from that of contractile protoplasm. But the muscular fibres are collected into great masses, permitting macroscopic investigations of a chemical and physical nature to be undertaken upon them which are not applicable to microscopic inquiries. The range and variety of experiments performed under the microscope is undoubtedly constantly enlarging, and consequently improved means will be hereafter obtained for acquiring a knowledge of the physiology of cells. At present, however, this must still rest on the physiology of muscle, as probably it will continue in great measure to do, even when it has received its greatest development. With regard to the specific functions of cells, we must limit ourselves to the general statement that there are cells possessing very various physiological functions, as nerve cells, muscle cells, gland cells, etc.; and, inasmuch as we are unable to conceive any functional process to take place in a cell without the occurrence of chemical processes, we must suppose that the specific functions of the cells in these several cases are essentially dependent on the nature of the chemical processes occurring in them. In the case of the muscles and in that of nerve cells, chemical investigations furnish us with no information beyond that of the dead tissue; whilst, in respect to gland cells, we do obtain some little insight into the nature of the chemical processes through an investigation of the secretion. Thus we know that there are cells which produce fat (mammary and sebaceous glands), others which develop pepsine, and further, that as a consequence of the activity of muscle and nerve tissue, acids are formed.*

From the results of the chemical investigation of protoplasm it would appear that, in all probability, it contains a considerable proportion of myosine (Kühne).† In some protoplasmic masses, protagon (Hoppe-Seyler, Fischer), in others glycogen, has been shown to be present, and in some few vegetable cells cholesterine‡ has been found.

It may be questioned, and remains to be shown, whether the

* Du Bois, Funke.

† See Kühne, *Lehrbuch der Physiologische Chemie.*

‡ Hoppe-Seyler, *Med. Chem. Untersuchungen.*

substances which are obtained from cells after their death are pre-existent in them during life, or are only the products of disintegration. Hermann is of opinion that myosin is one of these products of disintegration. Of the nature of the functions fulfilled by the water and other inorganic compounds that exist in protoplasm, we know absolutely nothing.

STRUCTURE OF CELLS.—Brücke* described a system of lacunæ in the salivary corpuscles, the cavities of which he thought were occupied by an intracellular fluid. He stated that the same appearances were presented by the protoplasm of the vegetable cells composing the stinging hairs of the nettle. Heidenhain† held the same opinion, and further maintained that the intracellular fluid was moved by the protoplasm in the same way that the contents of the intestines were propelled onwards by the peristaltic movements of the intestinal walls.

The protoplasm of vegetable cells may be so arranged that it traverses the space within the cellulose wall like a spider's web, and in such case the spaces between the protoplasmic fibres are occupied with a fluid; or the protoplasm may be reduced to a thin layer lining the inner surface of the cellulose wall, the interior of which again is bathed with fluid. But this cell fluid is not to be confounded with that which occupies the inner spaces or lacunæ of the protoplasm itself.

It may be observed in the flask-shaped glands of the nictitating membrane of the eye of the frog, that the size of the gland cells undergoes considerable variation. Sometimes the cells project so far into the lumen of the tube that this is reduced to an extremely small diameter; whilst, on the other hand, the cells are sometimes so contracted that the gland appears like a bladder lined with a simple layer of epithelium. These differences are not easy to comprehend, except on the supposition that the gland cells have by contracting expressed fluid from their interior.

It is also probable that at different times the protoplasm

* *Ueber die sogenannte Molecular bewegung.*

† *Studien des Physiologischen Instituts zu Breslau,* Heft ii.

contains a greater or smaller quantity of fluid, and that under particular circumstances—by contraction or shrinking—it may thus be reduced to extremely small dimensions.

Another question which remains to be solved is whether we have grounds for admitting that, independently of the intra-cellular fluid, there exist any differences in the structure of the protoplasm.

Optical examination has not as yet enabled us to draw any conclusion on this point. Hitherto protoplasm has only been observed to be a body refracting light singly; or, more correctly speaking, no part of it has been observed to possess doubly refractive powers. When such a peculiarity has been observed, the protoplasm has been considered to be modified in order to fulfil some special purpose.

I am myself inclined to believe that two functionally different substances are present, and am supported in my opinion by the circumstance that I have learnt to recognize two active conditions: one in which the cell is dilated, as after immersion in water; and one in which it is contracted (shortened).

But even if the dilated condition, as on Hermann's hypothesis, is to be regarded as the condition of rest, we must from this point of view also admit the existence of two functionally different substances.

In the present state of science we must acknowledge that we are unable to see any differentiation of parts under the microscope, nor does experiment furnish us with any ground for admitting the existence of a definite arrangement of parts differing in their physiological properties. At the same time, those cells, or cell derivatives, must of course be excepted in which we are able to recognize any definite peculiarities appearing to be associated with the performance of a specific function. The optical peculiarities of transversely striated muscular fibres, and the apparent structure perceptible in ganglion cells, must doubtless be regarded as dependent on differentiation of structure. Such instances as these are referrible to the class of protoplasmic masses modified for the performance of some special function.

In reference to the boundaries of a cell, the state of our pre-

sent knowledge has already been given in the introductory portion of this section. We hold that the external limiting layers of protoplasm may undergo both chemical and physical changes, and there will then be produced a membrane that, compared with protoplasm, is of firm consistence. The recognition of a double contour line in the uninjured cell is indispensably necessary to prove the existence of an investing membrane. Brücke remarks in reference to this point, "The difference between the density of the surrounding medium and the cell, even when no investing membrane is present, will cause the appearance of a boundary line. But it is only from the presence of a second contour that we are able to recognize a difference in density between the investing substance and the contained material. It is self-evident that the power of the instrument must not be pushed beyond its natural limits by the employment of strong oculars, as in that case a second contour line makes its appearance, not due to the structure of the cell, but consequent on defects in the optical apparatus we are using." If, moreover, a double contour line is observed after the action of reagents, no proof is afforded that a membrane existed during life. Kühne argued respecting the value of the double contour line as an evidence of structure, in the following terms: "If an amœba were to surround itself by a broad hyaline border, not regularly defined internally, I should not be surprised if a reagent like acetic acid, which made this border suddenly shrink whilst under observation, were to cause the appearance of two wrinkled, closely approximated contour lines; and if I knew that this border was previously mutable, I should not believe the solid membrane, originating in the action of acetic acid, was previously present as an investment of the outer hyaline layer."

Many cells of the integuments possess distinctly perceptible membranes, as in the case of the mucous cells on the surface of fresh-water fish, first described by Leydig, and in a series of other analogous structures which F. E. Schulze* has collectively designated cup or chalice cells. F. E. Schulze distinguishes two kinds of cells, in one of which the membrane (theca) is

* Max Schultze's *Archiv*, Band iii.

completely closed, whilst the other exhibits a roundish, sharply defined opening.

At a much earlier date the epithelial cells of the villi had already been described by Brücke* as destitute of a membrane at their free extremity. It is still a subject of dispute whether this is a characteristic of all the epithelial cells, or occurs only in certain cup-like organs scattered amongst the ordinary cells of the epithelium.

The cell membrane may appear perfectly homogeneous, or it may possess pores (Leuckart).†

The investing membrane may further present, according to F. E. Schulze, a want of homogeneity in consequence of becoming thickened by a secondary deposit. The basal part of the membrane of the epithelial cells of the villi, which is turned towards the lumen of the intestinal tube, must be regarded as a structure of this kind.

It is also here a disputed question whether this basal border is perforated by pores (Funke, Kölliker), or is composed of rods, giving it a striated appearance (Brettauer, Steinach).

The Nucleus of the Cell.—Since R. Brown discovered the existence of a nucleus in vegetable cells, no remarkable advance has been made in our knowledge of this structure. Both Schleiden and Schwann held that the development of cells proceeded from the cell nucleus, and before as well as after their time the nucleus has always been regarded as a structure playing an important part in the propagation of cells. The objections have been already stated that were urged by Brücke against the view that the nucleus must be admitted as an indispensable attribute in our idea of a typical cell. We, in fact, know nothing with certainty respecting its physiological significance, nor regarding its physical peculiarities. It is, indeed, well known that, as a general rule, when a nucleated cell divides, the division first proceeds from the nucleus, which elongates, becomes hour-glass shaped, and ultimately constricted into two segments. Brücke adduces this

* *Denkschriften d. Wien. Akadem.*, Band vi.

† See also F. E. Schultze, *loc. cit.*

as an answer to the statement, if any one were disposed to make it, that in all modes of propagation of cells the nucleus remains entirely passive. But in opposition to this line of argument is the fact that we are at present acquainted with non-nucleated cells capable of undergoing division, which is in itself a direct and sufficient answer to every statement that can be advanced in favour of the importance of the nucleus. It might indeed be said that when the nucleus is present it fulfils some important end in the act of propagation; but, in reply, it may be remarked that the division of nucleated cells has been observed where the nucleus has remained attached to the side. Remak* has made similar statements in regard to the red blood corpuscles, and very recently Weiss† also in reference to the protoplasm in the hairs of plants. Moreover, we know very little respecting the physical peculiarities of the nucleus. Reinhard has deduced its vesicular nature from its behaviour in water, but we now know how little value must be placed on deductions of this kind. The presence of an investing membrane in many nuclei can be contested on the same grounds that render the presence of an investing membrane in various kinds of cells doubtful; many nuclei appear to be completely homogeneous, and are distinguishable from the surrounding protoplasm only by a single well-defined contour. Nuclei are, moreover, capable of undergoing manifold changes in form, and these may either be of an active or of a passive nature. At the same time we know that processes of budding and other similar changes cannot easily be conceived to occur in a vesicle enclosed by a membrane: when an amœboid cell is pressed flat, the nucleus also is compressed; and if the cell be again allowed to resume its original form, the nucleus similarly changes its shape. These are peculiarities that are certainly not very consonant with a vesicular character; still it is true that in many nuclei a double contour can be distinctly shown, as, for example, in many ganglion cells. It cannot be doubted, also, that such nuclei are invested by a limiting membrane of different nature from the contents; but we have no right to draw the conclusion from this,

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* *Entwickelungsgeschichte.* Berlin, 1855.

† *Die Pflanzenhaare.* Berlin, 1867.

that the nuclei are usually vesicles. Rollett* some time ago paid particular attention to the nuclei of the corpuscles, and described a peculiar formation of vacuolæ in their interior. More recently it has been stated, on the authority of observations made in his laboratory, that after induction currents have been applied to the corpuscles the nuclei will coalesce, which is very unlikely on the supposition that they consist of vesicles.

Our knowledge respecting the chemical characters of nuclei is also very obscure. Kühne† states that it is probable they contain an albuminous substance, and it is known that they present considerable resistance to the action of acids and alkalies; but this furnishes us with no satisfactory information respecting their physiological significance or chemical composition. Brücke remarks that the consistence of the nucleus is peculiar. On the cell theory it is believed to constitute the primary solid constituent of the cell, though no absolute proof has been obtained on the point. It cannot be denied that the nucleus is originally of very soft consistence, and that it subsequently becomes denser; nor can it be admitted that it ever exhibits any considerable degree of resistance in young cells.

It has been stated that, in all probability, the nucleus of the fecundated egg disappears. It is equally probable that the nucleus of the first segmentation mass is a new formation. But, as we possess no precise investigations respecting the disappearance of the germinal vesicle, we are also unable to derive the first nucleus of the segmentation mass of the egg of the frog from the nucleus of the unfertilized egg. In the unfertilized egg we meet with a vesicular nucleus. Under a strong lens it may easily be torn with needles, and then the membrane becomes apparent. The small sacculus contains a little clear fluid and a few granules. The first nucleus of the segmentation sphere is, however, a completely homogeneous and apparently soft spherical body.

When it is said that the nuclear vesicles undergo solution,

* *Versuche am Blute, Wiener Sitzungsberichte*, 1863.

† *Lehrbuch der Physiologische Chemie.* Leipzig, 1867.

and are then again reformed, we have really not advanced one step in the solution of the question, for even this rests on no satisfactory evidence whatever.

What we do know is, that in its earliest stage the fertilized egg has no visible nucleus, and that the nucleus of the first segmentation sphere originates in protoplasm; that when very young, which must necessarily be its state in the segmentation sphere, the nucleus consists of a little mass of substance, in which, amongst other products of disintegration, albumen is found; lastly, that when old, and for this the unfertilized egg may be taken as an example, it may become converted into a vesicle.

Lionel Beale* has offered a plausible, though negative, explanation of the significance of the nucleus. He applies the term *germinal matter* "both to it and to protoplasm," and places them in opposition to *formed material* which constitutes the investing membrane. This view contains, at any rate, an indication that the nucleus and protoplasm possess certain characters in common.

Our knowledge of the nature of nucleoli is still more imperfect than that which we possess respecting the nucleus. To these also a special significance has been ascribed in the act of propagation, Virchow having quite circumstantially described his observation on the division of the nucleolus; and this, indeed, is the whole extent of our knowledge. Leydig refuses to admit that they are of any importance; but we cannot go so far as this, if we reflect that the nucleoli in many cases develop into a vesicle, in which still smaller nucleoli may be distinguished.

Cell Genesis.—Schleiden advanced the theory that plants originate exclusively in homologous constituents. He proved that the nucleated cell was the only original component of the embryo of the plant, and that the development of all tissues might be referred generally to such cells. The formation of these cells takes place in a plasma, the nuclei first appearing, and then the investing membrane. The formative material, however, is commonly found within previously existing cells.

* *The Structure of Elementary Tissues*, 1861.

Schwann, speaking of the origin of cells, remarks, "We have, in the first instance, a structureless substance, which, according to its chemical qualities and the grade of its vitality, possesses a greater or less capacity of effecting the development of cells."

Schwann was of opinion that the extracellular formation of cells, that is, their development in free blastema, was the most frequent mode of their production in animals. But the experience of embryologists was soon found to be in opposition to his views. The segmentation of the egg of the frog, already observed in 1824 by Prevost and Dumas, led to the statement made in the beginning of 1840, that the segments into which the egg breaks up are cells. This view was in the first instance defended by Reichert,* who believed that he was able to perceive a cell membrane in the several segments. Bergman† raised very solid objections to the existence of a membrane in this instance; and he quite correctly maintained that the spheres of segmentation are cells which are at first destitute of a cell wall, though they become invested by one at a subsequent period.

Henle also held that a close relation existed between the process of segmentation in the egg and the division of cells, and Kölliker interpreted the segmentation of the germ of cephalopods in the same manner. But this view of cell genesis was again very generally departed from. The merit of having defended it effectually must be ascribed to Remak‡ in particular, who has chiefly contributed to the abandonment of Schwann's doctrine of cell formation. Remak maintained with great steadiness that in the early stages of the development of the embryo no other mode of cell development occurs than by division.

To Remak also the merit is due of having established the same law in respect to the pathological development of cells. There is at the same time no doubt that Virchow played an important part in the extension of our knowledge in this direction,

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* *Entwickelungsgeschichte im Wirbelthiere*, 1840.

† Müller's *Archiv*, 1841.

‡ *Entwickelungsgeschichte*. Berlin, 1852–1855.

and that his well-grounded statement, made in 1855, "Omnis cellula e cellula," really constitutes the basis of our present cell theory.

Whilst these fundamental propositions respecting the mode of cell formation in compound bodies were advanced and maintained on the one side, Pasteur proved by brilliant experiments that the statements made respecting the spontaneous origin of various organisms in fluids were erroneous, and that when all access of living organisms into such fluids was prevented, no development could be proved in any case to occur. Every one must admit that the general tendency of these facts is to disprove that a free extracellular formation of cells ever takes place. At the same time we are not justified in maintaining that such a mode of formation never occurs; it may, however, be said that at the present time not one observation has been made, incontestably demonstrating the existence of a generatio æquivoca.

We distinguish three forms of cell multiplication, one by fission, one by gemmation, and, lastly, an endogenous mode. According to Brücke, the last differs from the two former in the circumstance that the cells originate like embryoes in the interior of the parent cell, and gradually increase in size, whilst in the other cases the substance of the mother cell breaks up into fragments, which constitute the second generation.

In the multiplication of nucleated cells by division the nucleus, as a rule, first divides; becoming elongated, then finger-biscuit shaped, and finally constricted into two portions, which recede from one another. The fission of the nucleus is not in all instances followed by division of the cell, though it is usually associated with the process of cell multiplication. Instances are known where cells become greatly enlarged, whilst their nuclei increase in number, either regularly or irregularly, to twenty or more; and in which, nevertheless, division of the cell itself has not been observed to occur. Division of the nucleus external to the cell, as has been already stated, has not as yet been shown to take place.

The formation of fresh nuclei within cells must be admitted

Virchow's *Archiv*, 1855, Band viii., Heft 1.

to proceed, not only from fission of old nuclei, but from the growth of entirely new ones.

Development of nuclei proceeds in a manner essentially similar to that of cells when they undergo complete division.

As an example of endogenous cell multiplication, that which takes place in the eggs of insects may, according to Weismann,* be adduced; but whether the formation of pus corpuscles in epithelia (Buhl)† is to be regarded as an example of this mode, or of division (Remak) is at present doubtful.

If the entire mass of proloplasm contained within a membrane or capsule divides into two or more segments, we can no longer regard this as an endogenous mode of cell division, but as cell genesis by fission. Cartilage cells and the first two segmentation spheroids may be adduced as examples.

When a naked mass of protoplasm divides, the act is obviously to be regarded as one of fission. As an example of this the fission of the eggs in the ovaries of young cats may be adduced (Pflüger).

In multiplication by gemmation a little elevation first projects from the cell—a bud—which is subsequently separated by constriction of its base. An example may be seen in the propagation of the yeast fungus, in the development of the egg in Nematoids (Meissner), as well as in the budding of the germ of many holoblastic eggs (Salmofario, Stricker). The detachment of a cell from the maternal structures is a phenomenon of movement (Max Schultze). In regard to cell formation by fission, it has been ascertained that the protoplasm becomes partially contracted in the fashion of an hour-glass. The depth of the constriction continuously increasing until at length the protoplasm is divided into two segments. The whole process

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* *Entwickelung der Dipteren*, 1864.

† The author of this paper has, as yet, had no opportunity to examine critically the communications made by Volkmann and Steudener, respecting the migrations of amœboid cells into epithelial cells, and the illusory appearances which may have led to the statement that an endogenous formation of cells take place in epithelial cells. He, however, fully maintains the correctness of the statements of Buhl in regard to the development of cells from pre-existent epithelial cells, and has consequently adduced it as an instance.

may be observed under the microscope in the fecundated egg of the frog.

No direct observations have been made as to the manner in which in endogenous cell genesis the daughter cells are set free in the body of the mother cell.

In many cases we are acquainted with the stimuli through the agency of which movements are occasioned. In the fecundated egg the spermatozoa must be regarded as the agents from which the first excitation proceeds. There can be no doubt, also, that in the act of fission a high temperature plays an important part (see above). In many other cases, however, the stimulus inducing the fission of cells is unknown.

The detachment of cells by constriction may be compared to the act of birth. Before detachment occurs by this mode the cell must have acquired a sufficient size, as otherwise material limits would soon be placed to the process of continuous fission. The essential feature of cell multiplication, therefore, consists in the capacity of assimilating new material.

The general proposition, then, that cells may increase by constriction and detachment, cannot be called in question. The segmentation of the ovum is an example which admits of no double interpretation. It may nevertheless be disputed whether certain cells of the adult organism are capable of increasing by constriction taking place in both the longitudinal and the transverse direction.

Since the migratory power of the white corpuscles has been ascertained, some doubts may arise whether any other cells besides these are capable of undergoing multiplication. With the exception of cartilage, in which there can be no more doubt of the occurrence of cell fission than in the fertilized egg, the structures which result from the fission of cells in the tissues of the healthy adult organization are not such as to render a mistake impossible. In cartilage we see the descendants of a parent cell enclosed in cavities of the solid matrix. But in all other tissues, where such firm boundaries are not met with surrounding families of cells, we cannot maintain with any degree of certainty that a group of two or four cells lying in close proximity to each other have originated in a previously existing mother of equal physiological value; for it might

happen in such a case that the cells have migrated thither from some other part. It is even conceivable that the colourless blood corpuscles are destined for the regeneration of all the tissues of the animal body. Nor can any solid objection to this view be raised from the stand-point gained by a knowledge of the history of development. The blood proceeds, indeed, from a different germinal lamina to the epithelia, for example; but primarily all cells proceed from the segmentation spheres, and these again from the fertilized ovum. Lastly, who can determine what influences must be in operation to cause a segmentation spheroid to become an epithelial cell, and whether similar influences may not also act on young cells in the post-embryonal period?

Epithelial cells with two nuclei are often seen, and it is generally taken for granted that the division of the nucleus precedes the fission of the cell; but who can say that every division of a nucleus is followed by fission of the cell? It is possible that the division of the nucleus in an epithelial cell may be only an instance of arrest of development occurring in a cell which is no longer capable of undergoing division.

At the time when this article was published, the doubt cast by Cohnheim upon the fact of the pus corpuscles arising from the cells of connective tissue and of epithelium, had an important influence upon the opinion of histologists in Germany. On this account the results of the investigations of Goodsir, Redfern, Virchow, and his pupils, were believed to be founded upon incorrect investigation.

My later investigations* have, however, shown that the process of division of pus cells can be directly observed under the microscope, and that the proliferation of the cells of connective tissue by division, and of those of the epithelium by endogenous generation, are facts which cannot be disputed.†

It has in the meanwhile been ascertained in the case of a very easily observed object—the blood-vessels—that they are partially able to regenerate themselves—that fine processes grow out from the capillaries, which are themselves capable of becoming capillaries.

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* *Studien aus dem Instituts für experimentelle Pathologie.* Wien, 1869.

† MS. note added by Prof. Stricker.

It is different with connective tissue. It cannot be doubted but that here some of the cells that migrate into it proceed from the blood; and the question must necessarily remain open, whether the connective tissue in those places where it maintains its ordinary local relations, is not usually regenerated by this means. W. Joung has expressed himself strongly in favour of this as being the mode of formation in the œdematous scrotum.

Our knowledge of the mode in which nerves and muscles are regenerated in the healthy organism is too limited to permit us to enter into any discussion respecting them. The main point of the question is connected with the growth of the gland cells, the epithelia, and the rete malpighii. Is the opinion justified, that the important discovery of Henle of the spontaneous growth of the rete mucosum can be shaken?

The development of epithelia from the cells of the connective tissue has already been maintained by many, as by Burkhardt, by Virchow, and by Förster. Very recently Pagenstecher* has stated that they may proceed from exudation corpuscles, and Biesiadecki says specifically that they come from colourless blood corpuscles. Two facts ascertained by the application of novel modes of investigation may lead to a decision on this point. The first is the presence of migrating cells between the epithelial cells (Recklinghausen), and the second the circumstance that after the injection of finely granular colouring matter into the blood, it is also met with within the epithelial cells. The last is not a fact of much importance, since particles of colouring matter can be floated to whatever part a current of nutritive matter may set. The presence of migratory cells is a more important circumstance, but is likewise not very weighty. No one has hitherto observed that the migrating cells become changed into epithelial cells; it is not really derogatory to us to say that we are still ignorant of the significance of the migrating cells, and that we do not know what becomes of them. Were any one to maintain that the migrating cells are conjugation organisms, no stronger objec-

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* *Wiener Sitzungsberichte*, 1868.

tion could be raised against him than against another who should maintain that the migrating cells are epithelia.

Recklinghausen* has advanced a theory respecting the conjugation of cells, which, however, on account of its brevity, scarcely allows us to judge of its value. The fact that the most beautiful example of cell fission, segmentation of the ovum, does not occur without fertilization, hardly enables us satisfactorily to determine the question whether the conjugation of cells is not a more frequent process than is generally admitted.

Forms of Cells.—No general statement can be made respecting the form of the amœboid cells, since the mutability of their shape is their distinguishing characteristic. It is to be presumed also that they present very different forms in death, and hence no certain conclusions can be drawn from the appearances presented by dead amœboid cells. These remarks are, however, only applicable whilst the cells remain suspended in fluid. In places where numbers are accumulated together they become flattened. Thus the segmentation spherules, whilst still in their natural position, are polyhedral with flattened sides, which are mutually opposed to the similar surfaces of others. Similar appearances are presented in most instances where soft and yielding cells completely fill a given space; but one axis may be longer than another, as is the case in the inferior layers of laminated epithelia, where they generally form prisms, or are arranged in the manner of palisades. The cells which are superjacent to them, on the other hand, are polyhedral, without any one axis being longer than another. The uppermost layers of laminated epithelia are usually flattened.

The cells of the laminated epithelium of the upper part of the respiratory tract are for the most part elongated, and present two principal varieties in form, one of which is that of a longer or shorter flask-like body, giving off a process from one of its ends, whilst the other is that of a fusiform cell with a relatively short belly and elongated attenuated extremities.

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* Max Schultze's *Archiv*, Band ii.

Where the cells line the interior of cavities as a single layer, they appear either in the form of plates of different shape (endothelial cells of His), or of cells in which the long axis is predominant (cylindrical epithelial cells); or we may meet with various intermediate forms between plates and cylinders.

The cylindrical cells are not cylinders in a stereometric sense, but are frequently conical, with the base turned towards the cavity, whilst at other times they form cones, from the apex of which a process is given off. Cells may again present the appearance of being as it is termed ramified, or provided with numerous processes (bone cells, corpuscles of the cornea); or lastly, they may become extraordinarily elongated as in muscle cells.

A form of cell which must be regarded as quite peculiar, is that which is provided with cilia. The form of the ciliated cell varies to a considerable extent, but the cilia are always limited to one portion of the surface, and constantly project with their free extremities into the interior of the cavity of the organ they line.

The cilia themselves may be of various length, and may on the one hand considerably exceed the long diameter of the cell, as occurs in those lining the renal capsules of some amphibia (Remak,* Duncan); and on the other may be so short that they only measure a fraction of the long diameter of the cell; it is in such cases especially that when at rest they give the appearance of a moderately broad hem or border to the cell. Again, not only the length but the thickness of the cilia varies; thus we find that the cilia on the superficial cells of the egg of the frog, after it has undergone segmentation, can scarcely be perceived even when magnified 400 times with a good instrument; whilst the cilia on the gills of the Anodonta are easily recognized near their base with a very low power.

Union of Cells with each other.—By the treatment of tissues with diluted solutions of nitrate of silver, as suggested by Recklinghausen, we have acquired a knowledge of the

* *Frorieps Notizen*, 1845.

† *Wiener Sitzungsberichte*, 1867.

means by which certain varieties of structure can be recognized, and we have also learnt that even when cells are apparently in contact an intermediate material is present, by which they are cemented to one another. Recklinghausen has by the use of this method rendered certain markings apparent in the finest lymphatics; and Eberth, Aeby, and Auerbach* have by similar means exhibited peculiar patterns in the blood capillaries, whilst similar lines may generally be brought into view wherever cells lie in apposition.

A difference of opinion exists in regard to the significance of the lines brought out by silver in the blood capillaries. Those who oppose the ordinary view base their opinion upon the history of development, from which we learn that the blood capillaries commence as solid fibres, and then become hollow; but we also know, through the investigations of Reitz,† that the villi of the placenta commence as solid fibres, which subsequently become hollow, and that after the occurrence of an abundant proliferation of nuclei the sheath of protoplasm of these now hollow processes undergoes differentiation into cylindrical cells. We thus see that a considerable mass of protoplasm can become differentiated into cells.

The formation of the blood capillaries must be described in a similar manner; they commence after the fashion of a gun barrel with smooth bore, but subsequently appear like the shaft of a chimney; cell boundary lines, or, more correctly speaking, lines of connective substance, being developed in their wall.

The consideration of this process teaches us that the cement is to be regarded as proceeding from the metamorphosis of the cell substance, and is therefore properly included in the series of intercellular substances. Cells may either present flat surfaces in apposition to each other, or they may present small processes, dentations, or striæ, by means of which they cling to one another like the bristles of two brushes.‡ They may also become attached to one another partly by means of flat surfaces and partly through the intercalation of the

* *Centralblatt*, 12, 13, 14, 1866.

† *Wiener Sitzungsberichte*, 1868.

‡ Max Schultze, *Centralblatt*, 1864, No. 12.

processes.* Inasmuch as the cement is included in the series of intercellular substances, it must be admitted that there is no fundamental morphological difference between the material connecting epithelial cells, endothelial cells, and the cells of the connective tissues; in all these we have to do with metamorphosed cell substance, by means of which the morphological elements are united.

Besides the mode of union by means of intercellular substance, we are also acquainted with a mode in which cells unite through the intermediation of processes, and we have already noticed that, under certain circumstances, cells may become fused together, an occurrence that may take place whilst they are yet living. We cannot therefore doubt that the protoplasmic masses are capable of directly uniting with one another. Nevertheless the microscopic proof of the direct fusion of cells has not been quite satisfactorily demonstrated. It is possible that the union may be established by means of cement, but this, up to the present time, has not been clearly shown.

From a physiological point of view, however, we must admit that fusion of the processes of nerve cells may take place; at all events, it would be in opposition to our experience respecting the conduction of nervous force, were we to admit that any cementing substance intervened between the individual nerve cells.

With the exception of the nerve cells, the above-mentioned objection holds good for all supposed or actually proved instances of cell union.

CLASSIFICATION OF CELLS.—Cells are usually classified in accordance with their physiological function. This, however, is not a very satisfactory mode, since we are still ignorant of the functions of many groups of cells. For example, we have no precise knowledge of the functions fulfilled by the colourless blood corpuscles, and it is moreover improbable that all the cells distributed over the surface of a membrane, as epithelial and investing cells, should possess identical functions. We find,

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* F. E. Schulze, *loc. cit.*

for instance, that between the epidermal cells of the fish there are peculiar clavate cells which have been described by Max Schultze, and circular-headed cells by F. E. Schulze; whilst wandering cells, chalice-like cells, etc., have been observed by others. All these forms of cells are probably functionally different, and cannot, according to our ideas of classification, be included under the single head of epidermal cells.

It has been thought that a primary ground of classification of cells might be drawn from some of their morphological characters or genetic peculiarities, but we shall see that none of these characters are sufficient to attain the end in view.

In reference to function we must distinguish nerve cells, muscle cells, red blood cells (respiratory organisms), gland or secreting cells, ciliated cells, and, lastly, connective tissue cells, as amongst those whose function essentially consists in the construction of the framework of the body. With these may also be enumerated those cells, the function of which we deduce from their situation and arrangement; to this group belong the cells of the epidermis, with the endothelia and those cellular investments of the mucous membranes to which we can ascribe no specific secretion, as the epithelium of the œsophagus and of the urinary tubuli. The function of these may be considered to consist in forming the boundaries of cavities, and in protecting important organs, as the cutis, against external injurious influences; but at the same time we must admit that in regard to their morphological differences we are but partially acquainted with their function. Lastly, the colourless lymph and blood corpuscles may be alluded to; of these we know indeed that in all probability they are destined for the regeneration of the red blood corpuscles, but we know also that they fulfil other and quite different objects.

Cells can be classified according to their genesis, that is, according to the germinal membrane from which they originate; nevertheless, however successfully the classification of investing cells into epithelia and endothelia (His) may be effected on this principle, it is not capable of wider application. The cells of the cutaneous glands, for example, would have to be separated from those of the intestinal glands, because the former proceed from the upper, the latter from the lower,

germinal membrane. Moreover, all cutaneous glands would have to be included in the series of epidermal cells, all epithelia in the series of secretory cells, and, lastly, connective tissue, muscle, and blood would require to be combined in one and the same category. If no objection can be raised to many of these systems of arrangement, it is at least impossible to regard any of them as perfect.

Morphological peculiarities alone constitute a ground for the formation of subdivisions, and these will be considered in subsequent chapters.

Formative Activity of Cells.—The recognition of the fact that the animal body, excluding the ingesta, consists only of cells, or of cell derivatives, constitutes one of the most valuable conclusions arrived at by Schwann.

The next chapter will place before the reader, in a more extended form, the facts on which he grounded this statement. We can here only refer to the general importance of cells in the animal body, and in regard to their formative activity it may suffice to point out that every organised portion of the animal body which is not a cell must originate in or from cells. In addition to the organised constituents of the animal body, chemical compounds are also present in it, which, so far as they have not been introduced in those forms, must be regarded as the products of cell activity; but we cannot ascribe the non-organised bodies, even though they may be deposited as solid compounds, to the formative activity of cells. To this account we only place those materials which become a portion of the organised constituents of the animal body through cell metamorphosis.

Changes of Cells in Death.—It is difficult in many cases to decide whether a cell still lives; it is not sufficient to know that the preparation has been taken from a living animal, or from the body of one which has only been dead for some hours. If the cells exhibit no amœboid movement, and if, on the other hand, they are not taken from putrefying portions of the body, the determination is difficult, and sometimes even impossible. In the present state of our knowledge, chemical reagents do

not enable us to arrive at any positive decision, unless their action is sufficiently slight to excite movements, but not to effect complete destruction. This is indeed true of all other agents, for they can only furnish us with information in regard to the life of the cell when they produce changes which our experience teaches us are ascribable to life; on the other hand, it is often easy to determine that a particular cell is dead. The greater number of chemical reactions refer to the phenomena exhibited by dead cells. The forms which cells killed by chemical agents present are so various that they cannot be enumerated, but the most important have been treated of in the first chapter.

If the cells have been killed by powerful electric currents, by a high temperature, or by mechanical violence, the determination of their condition, after what has already been said upon the effects of these agents, can no longer be doubtful. But if no remarkable alterations of form (flattening, tearing, bursting), no remarkable physical alterations (cloudiness, coagulation), and lastly, no definite change resulting from the action of the fluid in which they have been preserved, furnish indications of the death of the cells, no scientific value can be attributed to any statement made respecting it.

CHAPTER II.

THE CONNECTIVE TISSUES.

By A. ROLLETT,

PROFESSOR OF PHYSIOLOGY IN GRAZ.

It has become customary in histology to associate together a series of tissues under the term connective tissues. From these tissues all those portions of the animal body are formed, which can be regarded in the most general significance of the terms as the basement membrane, supporting layer or investment for epithelial structures, blood, lymph, muscles, and nerves. In the Vertebrata the group of connective substances includes connective tissue, cartilage, bone, the tissue of the cornea and dentine.

The connective tissues are developed from the middle germinal layer, in which blood and muscle also originate. The typical connective substances are recognised histologically by the circumstance that they contain extensive and continuous layers of material (intercellular substance), which, when compared with the cellular structures distributed through its substance (protoplasma), or the morphological elements in other tissues, always appears as a more passive substance, and one which participates but slightly in the processes characteristic of life. These masses consist for the most part of gelatine-forming substances, such as collagen, chondrogen, and ossein. The connective tissues frequently pass by substitution or genetic succession into one another; they appear therefore to be morphologically equivalent; so that in many instances certain organs, or parts of organs, belonging to animals nearly allied to one another, are formed sometimes of one, sometimes of another of these tissues.

Even if our knowledge of such facts disposed us to collect the tissues into a single category, this is still not the immediate and primary reason that has led to the formation of a group of connective substances. This last has become customary since the experimental investigation of these tissues has shown that they present similar modes of development, and possess consequently an homologous significance in regard to their microscopic constituents.

The fate of the connective tissue theories thus originating has been very variable. Reichert* first appeared with his doctrine of continuity of substance. According to this the connective tissues contain a matrix, originating in the fusion of cells, or of certain portions of cells, with an amorphous intercellular substance. Reichert associated with this mode of development the peculiar connective tissue formerly regarded as fibrous, but considered by him to be destitute of structure, and pointed out that in both there was an absence of any apparent boundary line between the allied tissues where they were in contact with one another, or, as he expressed it, there was a "continuity" of their matrix.

This theory was, even from the first, strongly opposed by Henle,† and did not in the first instance meet with general acceptance. If the views on the absence of structure in connective tissue taught by Reichert, and now disproved, found certain adherents, amongst whom Virchow himself may be included, it can scarcely be held, as however is frequently done, that the connective tissue theory promulgated by Virchow in 1850, was only a modification of that of Reichert. We are indebted to Virchow‡ and Donders§ for directing attention to the persistence of cells in mature connective tissue. Virchow, whilst he regarded the cells of connective tissue (connective tissue corpuscles) as the analogues of the cells of cartilage and bone, constructed a simple scheme||

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* *Beiträge zur vergleichenden Naturforschung*, etc., Dorpat, 1845.

† Canstatt's *Jahresbericht*, 1845, Bd. i., p. 55.; 1847, Bd. i., p. 44.

‡ *Würzburger Verhandlung*, Bd. ii., pp. 154 and 314.

§ *Zeitschrift für wissenschaftliche Zoologie*, Band iii., p. 348.

|| *Cellular Pathologie.*

for the structure of connective tissues; and, upon the other hand, sought to attribute to the excitation, growth, and proliferation of these tissue cells a series of the most important pathological processes, and was thus led to the profound views contained in his cellular pathology.

According to Virchow's idea the greater part of the tissues belonging to the group of connective tissues consists of intercellular substances, the latter indeed varying in regard to their chemical nature in the several members of the series, and containing variously formed but similar cells imbedded in their substance. The views of Virchow obtained general acceptation. The special methods which he employed in his researches caused him, however, to describe forms which had nothing to do with connective tissue cells, and induced him in the case of connective tissue, as had been done by earlier inquirers in regard to osseous tissue, to admit the existence of cell processes frequently anastomosing with one another, which he regarded as forming a plasmatic canal system traversing the tissue in all directions. Henle* in both instances expressed determined and persistent opposition to the existence of connective tissue corpuscles in the sense understood by Virchow. The point in question required an exact appreciation of appearances exhibited under the microscope, and the final result was that inquirers for the most part convinced themselves of the existence of persistent cells in mature connective tissue.

In the meanwhile, however, through the investigations of Max Schultze,† Brücke,‡ and others, the doctrine of cells founded by Schwann, and up to that time generally received, experienced some important modifications. It was no longer possible to describe animal cells as uniform elementary parts of a vegetative character, constructed according to a certain scheme. The new opinions held in regard to the structure of connective tissue substances could not remain without influence upon the general conception of a cell. Still more directly was

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* Canstatt's *Jahresbericht*, 1851, Bd. i., p. 22; 1852, Bd. i., p. 20; 1853, Bd. i., p. 8. See also Henle, *Jahresbericht* for 1858, p. 53; 1859, p. 28.

† Reichert and Du Bois Reymond's *Archiv*, 1861, p. 1.

‡ *Sitzungsberichte der Wiener Akademie*, Band xliv., 1861, p. 381.

the connective tissue question affected by the views which were coincidently expressed by Max Schultze upon the solid intercellular substances of the animal tissues. Up to that time the majority of observers regarded the matrix of hyaline cartilage as the prototype of an amorphous intercellular substance, and indeed very generally as the starting-point for its consideration. Max Schultze, on the other hand, opposed to this the hitherto little regarded views of Remak and Fürstenburg, on the matrix of cartilage, and sought to show that we have not here to deal with an intercellular substance in the sense of a hardened secretion between the cells, but rather that the so-called intercellular substance, from its very commencement, proceeds from the protoplasm of the cells. This, in its turn, immediately led to renewed investigation respecting the genetic significance of the matrix of bone, and of the fibrillar substance of connective tissue.

Max Schultze* forthwith stated his opinion that the fibrillar substance of connective tissue originates from "embryonal cells composed of protoplasm, and destitute of any investing membrane, which have amalgamated with one another." A thin layer only of the protoplasm remains lying around the nucleus of the primary cell, representing with this nucleus a connective tissue cell, destitute of cell wall (connective tissue corpuscles). It should also be mentioned that, quite independently of the discussion maintained on these points in Germany, similar views respecting the development of connective tissue were expressed in England by Beale.† According to Beale's peculiar terminology, connective tissue is originally composed of elementary parts (cells), which consist of germinal matter (Keimstoffe, protoplasm); but subsequently a part of the germinal matter is converted into formed material (in connective tissue the fibrillar substance), which was itself in the first instance germinal matter, and was developed at the cost of that matter. Beale, whose statements were of a somewhat general nature, admitted a similar genetic relation

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* *Loc. cit.*, p. 13.

† *The Structure of the Simple Tissues of the Human Body*, translated into German by V. Carus. Leipzig, 1862, pp. 36, 96, etc.

between the matrix of bone and cartilage, and the cells of those tissues.

Waldeyer* especially endeavoured to confirm these views, in the case of bone, by his beautiful researches on the process of ossification. It is obvious that, in the event of the above-described mode of development being demonstrated in the several cases of bone, cartilage, and connective tissue, a similar genetic agreement for all these tissues, though undoubtedly in a different sense from that advanced by Virchow, would also be obtained. But to what extent satisfactory replies have been given to these questions will hereafter receive consideration when these tissues are severally described.

As observers gradually acquired these views respecting the histogenesis of the connective tissue substances, a new starting-point for important general considerations respecting the living processes taking place in connective tissue was obtained, in quite another mode, by the investigation of living connective tissue. Von Recklinghausen† demonstrated that, in living connective tissue, cells are present which agree in their characters with the white blood corpuscles (lymph or pus corpuscles), and, in consequence of the amœboid movements they are capable of performing, constantly change their situation in the tissue. Von Recklinghausen further proved that when suppuration occurred in connective tissue, in opposition to the doctrine propounded by Virchow of the formation of pus by multiplication of the tissue cells, a migration of these movable cells from without into the substance of the tissue must be admitted to take place. These facts have attracted a proportionately greater interest since Stricker‡ established the permeability of the walls of the vessels for red blood corpuscles. Cohnheim,§ indeed, has recently referred to the older observations of Waller|| on the relation of the white blood corpuscles in inflammation, which have hitherto remained unnoticed; and, supported by these

* *Archiv für Mikroskopische Anatomie*, Bd. i., p. 354.

† Virchow's *Archiv*, Bd. xxviii., p. 157.

‡ *Sitzungsberichte der Wiener Akademie*, Bd. lii., p. 379.

§ Virchow's *Archiv*, Bd. xl., p. 1. Kosinksi, *Wiener Med. Wochenschrift*, No. 56 and 57, 1868.

|| *Philosoph. Mag.*, Vol. xxix.

older and his own more recent observations, has propounded the view that purulent infiltration really consists only in the migration of colourless blood cells through the vascular walls into the tissues. The relations thus shown to exist between the blood and the tissues must, as we shall see, still be held in view in discussing other questions bearing upon the connective tissue substances in the following pages. For this reason, the three typical connecting substances—connective tissue, cartilage, and bone—will now be separately described. The consideration of the peculiar tissue of the cornea, on the other hand, with dentine, and some others, will, on account of their more limited and special distribution in certain organs, be postponed to a later period.

Of Connective Tissue.

A series of various forms of tissue must be included under the term connective tissue. This name was originally given in 1830, by Johann Müller,* to the tela cellulosa of the older anatomists; but as at that time observers† had already convinced themselves that this tissue is essentially composed of very fine fibres, which may be proved to be the chief constituent of tendons, ligaments, membranes, and other formed portions of the organism, all these tissues, together with the tela cellulosa, were included amongst those portions of the organism which are composed of connective tissue. Formerly, however, the description of this tissue was limited to a fibrous form of the tissue, possessing very definite histological and chemical characters.

This limitation has, however, been greatly extended by custom, and just as, in consequence of their functional agreement and continuity of substance, a series of microscopically different structures are combined under a common term—as muscle, nerve, etc.—we are on similar grounds led to a general application of the term connective tissue, and to distinguish its

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* *Handbuch der Physiologie*, Bd. i., p. 410. Coblentz, 1835.

† Jordan. For the doctrines of G. F. Treviranus (1816), H. Milne Edwards (1823), see E. H. Weber's edition of Hildebrandt's *Handbuch der Anatomie*. Braunschweig, 1830.

several forms. Amongst the microscopic morphological constituents thus distinguishable in connective tissue may be enumerated cells; networks and trabeculæ, developed from cells consisting of peculiar delicate unbranched fibres (connective tissue fibrils), for the most united into fasciculi; and, lastly, fibres which are differentiated from those above named by the resistance they offer to the action of acetic acid and alkalies, by their repeated division, by their forming networks, and by their fusing into lamellæ (elastic fibres).

Of the Cells of Connective Tissue in General.

In all connective tissues, whether obtained from an adult organism or from one in process of development, cells may be found, the number of which in different instances varies within very wide limits. In the cells obtained from connective tissue we observe so many different conditions of activity, development, metamorphosis, and disintegration, and know so little respecting their material composition and changes, their physiological peculiarities, and their genetic connection, that it is impossible to give a general description, which shall be applicable to all the forms they present. On the other hand, a few facts may be here stated which are of general importance in regard to the cells contained in connective tissue, and will thus enable us to take a broad view of the subject; and, in the first instance, the researches commenced by Von Recklinghausen * and Kühne † on the living tissue may be adduced.

In the living body the cells of connective tissue may be observed wherever it is possible to make thin sections adapted for high magnifying powers quickly, and without the employment of any hardening process. They may then be subjected to microscopic investigation, after the addition of some indifferent fluid, as serum, the aqueous humour, and serum containing iodine, especially with the aid of a moist chamber. In specimens so prepared, Von Recklinghausen first observed the pre-

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* *Loc. cit.*

† *Untersuchungen über das Protoplasma und die Contractilität*, p. 109. Leipzig, 1864.

sence of migrating cells in the connective tissue; and after he had demonstrated that the cells of pus possess amœboid characters similar to those which were already known to exist in the white blood—and lymph—corpuscles, he pointed out that pus corpuscles lying in this tissue—as, for example, in the inflamed cornea or in the mesentery of the rabbit—possessed the same mobility. He further found that young cells, agreeing in their characters with the white blood corpuscles, are present in small numbers in the healthy cornea of the eye, in the tail of the tadpole, in the peritoneum, and in various other places.

Where such cells are found in connective tissue, they are characterised by their relatively rapid change of form, and by their coincident and considerable changes of place in the tissue, on which account they were designated migrating or wandering cells* by Von Recklinghausen. In regard to these cells, we must refer to the general doctrines of cells already given, and to the section on the blood. It may, however, here be remarked that they may be easily differentiated from other movable cells occurring in the animal body. Amongst the various cells present in the connective tissue of the fully developed and adult organism, these white blood-corpuscle-like cells are best characterised by the circumstance that they alone deserve to be named amœboid cells. These cells, if the expression may be allowed so, are the most active, and present the most variable forms that are ever observable in this form of tissue. From the researches which Stricker† made on the permeability of the walls for the morphological elements of the blood, and those of Cohnheim‡ and Hering§ on the exit of the white blood corpuscles through the vascular wall into the tissue, the derivation of the migrating cells of the connective tissue from the blood has been certainly demonstrated in some particular instances, and rendered highly probable for all.

The migrating cells may be most conveniently observed,||

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* *Wandernden Zellen.*

† *Sitzungsberichte der Wiener Akademie*, Bd. lii., p. 379.

‡ *Loc. cit.*

§ *Sitzungsberichte*, Bd. lvi., p. 691.

|| Von Recklinghausen, *loc. cit.* F. E. Schulze, *Archiv für Mikroskopische Anatomie*, Bd. ii., p. 378.

and differentiated from the other cells contained in the tissue, in the tail of the living tadpole. In this object Golubew has frequently exhibited to me the migration of these structures from the vessels.

In the case of the blood of the frog, it may be shown that the amœboid cells it contains are subservient to the regeneration of the red corpuscles, into which they become transformed by a process all the stages of which may be completely followed.* We must therefore ask whether any further metamorphosis occurs in the amœboid cells of the connective tissue; and on the answer we obtain depends the still more important question, whether all or much of the development and growth of connective tissue is to be referred to a proliferation of the cells forming the original mass of the tissue, or whether, as has already been shown to occur in neoplastic pathological formations, those amœboid cells participate which originate in localized germ masses in the organism, and have then migrated into the tissue.

We now turn to those cells of the connective tissue which are capable of being distinguished from the amœboid cells, and meet, in the first place, a peculiar material obtained from the living tissues, which has been made known by the researches of Kühne.† I allude to that kind of connective tissue which appears in the form of perfectly transparent membranes between the muscles of the leg and thigh in the frog. According to Kühne, several varieties of cells can be here distinguished, differing from the migrating cells. They all appear to be formed of granular material, but some are characterised by being surrounded with a very finely granular cloud, by which they are distinguished from the transparent matrix; that is, traversed only by a few fibres. Others, again, appear to be formed of a material containing larger strongly refractile granules. The coarsely granular cells possess, for the most part, an elongated form ; the nucleus, which occupies the broadest

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* Golubew, *Sitzungsberichte der Wiener Akademie.* Sitzung vom, 16th April, 1868.

† *Untersuchungen über das Protoplasma und die Contractilität*, p. 109. Leipzig, 1864.

part of the cell, is elliptical, transparent, and bounded by a double contour line, or it may appear in the thickened portion of the cell, indistinctly defined, and equably covered with the granular mass. It may be noticed that such coarsely granular cells are often connected by their apices in twos and threes together. Besides the fusiform coarsely granular cells, there may frequently be seen similar cells of more compressed and rounded form.

The finely granular cells are either provided with a distinct oval and clear nucleus, or their contents may appear to be accumulated at one point around a body resembling a nucleus. The finely granular cells give off a variable number of processes differing in their length and thickness; and these, radiating in various directions, frequently join. When these finely granular cells are long and carefully observed, slow changes of form may be seen to occur; such changes are, however, much slower than those undergone by the migratory cells, and do not lead to any remarkable change of place. In the same preparation, migratory cells are also frequently seen, and the difference in the mode in which the movements are performed, as well as other peculiarities of both forms of cells, may be easily ascertained by direct comparison. The migratory cells are generally smaller, and the addition of acetic acid brings one or several small round nuclei into view, whilst all other cells, after the action of acetic acid, present distinct nuclei of larger size and more oval form.

Kühne has endeavoured ineffectually to excite movements by means of electricity in the different kinds of cells he has described. If we apply a large induction apparatus (brought into activity by means of chromic acid and carbon, with a primary coil of 160 turns, a nucleus of iron wire, and a secondary coil of 6,245 turns, thrust quite home), and examine the effects of a few shocks, allowing a few minutes to intervene between each, it will be seen that the cells with finely granular protoplasm, withdrawing their finer processes, contract gradually into round strongly granulated masses; or they may only retract their longer processes to a certain extent, without causing them entirely to disappear, so that they become knotty, whilst the body of the cell containing the nucleus

assumes a rounded form. A return from this altered condition to the original form has not been observed. The above-mentioned appearances constitute a further difference, distinguishing these from the migratory cells; the latter show, as in the case of the white blood corpuscles, when such shocks have been transmitted through them, an alteration in their mode of movement, or a sudden retraction of all the processes, and the assumption of a round form; after which they soon again recommence their former movements (Golubew).* In similar preparations from newts and salamanders, the appearances presented are the same as in the frog. In warm-blooded animals, a loose connective tissue can be obtained from the surface of the muscles in the form of thin laminæ; this contains, indeed, a larger number of fibres than in the frog, but is nevertheless well adapted for the observation of the cells that accompany it. The masseter of a recently killed rabbit or guinea-pig may be exposed, and after division of the fascia a portion of the connective tissue immediately investing the muscular fibres may be removed with scissors, and in this coarsely granular and cylindrical protoplasmic masses may be seen, containing a more or less distinct elliptical nucleus. Most of these cells contain a few granules of considerable size, which in one focus appear as dark pigment molecules, and in another seem to possess a bright centre.

Besides these coarsely granular cells, other very finely granular ones appear, which are for the most part more delicate and pale, and frequently exhibit fine radiating strongly refractile striæ of greenish tint. These easily overlooked, delicate, and proportionately large structures may best be recognised by their very distinct large vesicular nuclei.

Cells similar to those above described may also be found in the looser connective tissue of other muscles, in the subcutaneous tissue, and elsewhere.

If we pass from the examination of such delicate and loose connective tissue to the thicker and denser masses of the same tissue, various objects may be found which are adapted for its examination in a physiologically fresh condition. For this pur-

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* *Loc. cit.* See the chapter *On the General Doctrines of Cells.*

pose the thin fasciæ of the frog and of warm-blooded animals are very appropriate, as are also the thin flexor tendons of the fingers and toes of the frog, newt, or salamander, which can be drawn out at one end from the double-capped fingers or toes. We may here see small fusiform granular masses containing delicate elongated nuclei intercalated amongst the parallel fibres of the several fasciculi. In comparison with the cells of the looser connective tissue, the granular substance of these cells appears to be much reduced in amount. In the above-mentioned tendons there also appear more rounded, serially arranged, and somewhat flattened cells with well-defined round nuclei. These do not lie upon the surface, but in the elongated fusiform interstices of the fibrous material. Such chains of cells have their greatest dimensions in the broadest part of the fusiform spaces. At the border of the above-mentioned tendons a thinner portion of the investing connective tissue is generally to be found traversed by numerous fibres in which the above-described cells of the loose connective tissue can be very well observed; but besides these, stellate cells may also be seen, which give off sharply bordered trabeculæ, that present a smoother appearance, give off branches, and may be followed for a considerable distance between the fibres of the investing connective tissue. The behaviour of the cells present in connective tissue, when treated with chemical reagents, now requires a more extended examination.

The migratory cells are best adapted for investigation in this respect, on account of their having been already so long known as the white corpuscles. In regard to other cells, the observations made by Kühne on his specimens may be adduced. Water acts energetically on the finely granular cells in particular, the granular material contracting around the nucleus, and only remaining connected with the surrounding parts by means of a few anastomosing processes. The meshes of the network thus formed are clear, and a few granules presenting molecular movements may be observed in their interior. The nucleus first swells up, and exhibits vacuolæ in its interior, and, after undergoing many changes of form, finally contracts into a shrivelled corpuscle.

The network brought into view by the action of acetic acid is darker, and the nucleus subsequently appears to be filled with dark granules.

In diluted solutions of potash and soda the nuclei of all the cells in such specimens are distinctly defined. They appear pale and vesicular. The cells acquire a border, seam or doubled margin; the granular portion of the cell diminishes in size with the formation of larger or smaller clear drops, and, in consequence of the coalescence of these drops, vacuolæ become developed, the formation of which was also observed by Kühne after the action of diluted acetic acid.

As has been above stated, but few objects are well adapted for the examination of connective tissue in the fresh state. In the case of all thick, soft, and easily alterable masses, or in those that are more dense and opaque, in order that the cells may be exhibited, preparations must first be made by section, or by teasing up the tissue with needles, and subsequently agents employed by which they may be hardened and rendered transparent. The objects that are capable of being examined in a physiologically fresh condition may then be used as test objects, and a comparison instituted between them.

The best solutions are those of chromic acid, and especially that recommended by Müller,* consisting of two and a half parts of chromate of potash, one part of sulphate of soda, and 100 parts of distilled water. If the latter be applied to the test object, which has just been obtained in the perfectly fresh condition, treated only with an indifferent fluid, and placed in a moist cell, it may remain as long as may be desired in contact with the reagent, and the changes produced by the hardening solution may be examined from time to time. We may then convince ourselves that Müller's solution preserves the cells in a nearly unaltered condition, so far as regards their external appearance. They indeed become slightly shrivelled, and the contour lines become smoother and more sharply defined; but the larger processes of the cells are completely preserved. The granular character of the cell substance be-

* See also Langhans, *Würzburger Naturwissenschaftliche Zeitschrift*, Bd. v., p. 86.

comes somewhat more distinct; but there is no more evidence of the presence of a membrane investing the cells as indicated by a double contour line now than in the fresh state. In all the cells the nucleus either becomes distinct, and presents a vesicular appearance with a coagulated mass in its centre, or loses its double contour, and appears coarsely granular throughout its whole substance. The imbibition of a solution of carmine renders these appearances still more distinct. From such hardened connective tissue, isolated cells may be obtained by teasing out the tissue with needles, and they may then present very various forms. The most common is the fusiform, very beautiful specimens of which may be obtained from the tendons of children and young animals, where they are both more numerous and more easily isolable than in those of adults,* and also from the connective tissue sheaths of the nerves in man and mammals. They may be obtained with equal facility from the neurilemma of the nerve trunks of frogs, still better from salamanders and tritons, and best of all from the proteus, where they are extraordinarily large, and can be isolated with the greatest ease; such isolated fusiform cells often possess very long nuclei, which are covered only by a thin layer of cell substance. Fusiform cells of remarkable size may be obtained from the tendon of the sterno-radial muscle (pre-sterno-clavi-radial of Dugés). They are here of a greater length than in any other tendon of the frog, and with their elongated nuclei call to mind smooth muscular fibre. The nucleus of these cells is on the average 0·0192 millimeters long and 0·0032 millimeters broad. Their length is difficult to determine, on account of both extremities ending in very fine and long processes. I found the length of cells, which had been completely isolated from the surrounding fibrous mass, to be in some instances as much as 0·0960 millimeters. In the tendons of man, isolated fusiform cells were 0·0320 millimeters long; the length of the nucleus amounted to 0·0160 millimeters, and its breadth to 0·0048 millimeters.

The cell substance of the fusiform cells is broader in young

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* Langhans, *loc. cit.* Grussendorf, *Zeitschrift für Rationelle Medicin*, 3 R., Bd. xxiv., p. 186.

animals and in embryoes, and here the cells frequently give off branched processes, which communicate with those proceeding from other stellate cells. The fusiform cells are less abundant in the fasciculi of the connective tissue of adults than was formerly supposed. They are remarkably developed in the cornea. In embryonic connective tissue they are very numerous, and repeatedly communicate by means of their processes.

We also meet with anastomosing stellate cells in the adult in the more independent connective tissue formations, occupying the interspaces of the fibrous connective tissue, or in places where fibrous connective tissue is altogether absent. From a general review of the cellular structures found in connective tissue, it is apparent that, beginning with the young cell, we have to deal with a series of cells in various stages of development.

The importance of any statement made in regard to the size and form of the cells, on which so much stress was formerly laid, will be less in proportion to the degree of mobility possessed by the cells when in the perfectly fresh condition.

It would, however, be decidedly going too far, were we to give up all distinguishing marks derived from the consideration of these points, since all experience tends to show that a distinction must be drawn between processes of protoplasm thrust forth by vital movement, and capable of being again withdrawn, and the fixed outgrowth of cells. The genetic connection existing between the various kinds of cells found in connective tissue, their physiological peculiarities, the chemical and physical alterations which they undergo from their first origin to a certain period of their life, etc., are all questions which require further investigation.

Lastly, The *pigment cells* of connective tissue require to be specially mentioned. In Man and the higher Vertebrata they occur only in a few limited spots, but they are much more widely distributed in Amphibia and Fishes, appearing especially in the skin, in the serous membranes, and in the tunica adventitia of the vessels.

In these places the pigment may also be found deposited in the form of granules which differ both in shape and colour.

The pigment cells of connective tissue are for the most part characterised by their beautiful stellate form, and by their numerous processes.

In man, in whom such pigment cells occur normally only in the eye, the pigment granules are of black or brown colour. The substance of which they are composed, and which is termed Melanin, is still but little known in regard to its chemical qualities. The granules are not perfectly round, but subcylindrical, or elongated with rounded extremities. They more or less completely fill the interior of the stellate pigment cells of the eye. As a general rule the ends of the cell processes remain colourless. The nucleus of these cells, in some cases, occupies the middle of the cell, and appears bright and distinctly defined; it contains no pigment, as is also the case with the cell substance which bridges over the broad side of the nucleus, whilst the cell mass lying around the nucleus, and its processes, are closely packed with the pigment molecules, so that the position of the nucleus appears as a clear space. In the stellate cells of the iris, and of the choroid of man, the pigment granules are most abundant shortly after birth.* Pigment cells also occur in the innermost layer of the sclerotic. In many animals, isolated pigment cells are thickly disseminated throughout the whole thickness of the sclerotic. Movements have been observed in the stellate pigment cells (chromatophores) of Amphibia,† and Fishes.‡ The pigment granules sometimes appear collected into round masses, and at others are diffused in the cell processes, which are often prolonged to a considerable distance. The movements observed are exceedingly tardy in adult frogs, but in the embryoes of these Batrachians they are somewhat more active.§ The spontaneous changes of form of the pigment cells in the skin of these animals, or those which are called forth by changes in the intensity of the light, are connected with the phenomena of change of colour which they

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* Brücke, *Anatomische Beschreibung der menschlichen Augapfels.* Berlin, 1846, p. 20.

† Brücke, *Denkschriften der Wiener Akademie*, Bd. iv., p. 23.

‡ Buchholtz, Reichert and Du Bois' *Archiv*, 1863, p. 74.

§ Büsch, Müller's *Archiv*, 1856, p. 425.

present.* Von Wittich† has described the effects of electrical excitation of the pigment cells of Hyla arborea, which appear to be most sensitive to it.

In adult specimens of Rana esculenta and temporaria, and also in Tritons, notwithstanding repeated trials, I was unable to perceive that any influence was exerted on the pigment cells by the action of induction shocks of electricity. R. Wagner has observed the presence of stellate pigment cells possessing extraordinary motility in Cephalopods.

THE VARIETIES OF CONNECTIVE TISSUE.—In its first formation, and during the earliest stages of its development, connective tissue consists of cells which, for the most part, lie closely compressed together; it then presents a parenchymatous appearance, similar to that observed in the embryonic tissue of certain neoplastic formations, as the small-celled sarcoma of Virchow.‡

Apart from this form of connective tissue, to which we shall again refer in the history of its development, that of the adult organism can be arranged under two heads; one of which includes those varieties of networks and trabeculæ that are developed from cells, whilst the other includes the fibrillar connective tissue, characterised by the presence of peculiar invariably unbranched fibres (connective tissue fibrils) composed of a gelatine-yielding substance.

Connective-tissue Plexuses and Trabeculæ.—These forms do not yield gelatine on boiling. They either occur in large independent masses, or they contain other tissues, to which they give support and covering, in the lacunæ of their meshes, which are sometimes more delicate and sometimes coarser.

a. In the former case the connective tissue is usually characterised by its succulency and its ready compressibility. The larger masses are transparent, or at least very translucent, and on section, in consequence of the escape of fluid, easily collapse (gelatinous tissue of Virchow). On the addition of acetic acid, a flocculent and threadlike precipitate of Mucin can frequently be obtained in considerable quantity from the escaped fluid

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* Brücke, *loc. cit.*

† Von Wittich, Müller's *Archiv*, 1854, p. 41.

‡ *Die Krankhaften geschwülste*, Bd. ii., p. 224, fig. 140.

which is again dissolved on adding an excess of the acid (mucous tissue, Virchow).* The morphological constituents of the tissue consist of delicate and soft cell structures containing nuclei, from which smooth trabeculæ are given off in various directions, that branch and anastomose with one another. Or there may occur in place of the cell plexus a delicate network of smooth non-nucleated trabeculæ, which present enlargements at the points where they intercommunicate. A larger or smaller number of amœboid cells are discoverable in the amorphous substance lying between the fully developed cells.

The tissue of the jelly-like substance of the umbilical cord described by Wharton, as it appears in the earlier periods of the development of the embryo, is to be reckoned amongst these forms. At a later period, especially in preserved specimens, a not inconsiderable quantity of the original tissue may be found, associated sometimes with fasciculi of fibrils, agreeing with those that, as we shall subsequently see, compose the fibrillæ of connective tissue.† The substance which occupies the Sinus rhomboidalis of birds is usually regarded as belonging to the mucous or gelatinous form of connective tissue; and a similar material is frequently met with in fishes, especially in the electric and pseud-electric organs; in the vicinity of the mucous canals of the Sturgeon and Plagiostomata, in various parts of the body in the Carp, Tench, Dace, and Eel, and beneath the sclerotic.‡ The vitreous humour of the eye may also be regarded as an example of it. The presence of gelatinous tissue has also been demonstrated in the Invertebrata, Heteropods, Medusæ, etc.§

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* *Würzburger Verhandlungen*, Band ii., p. 160, *Cellular Pathologie.*

† Henle, *Jahresbericht für* 1858, p. 61, *et seq.* Weismann, *Zeitschrift für Rationelle Medicin*, Band xi., 3 R., p. 140. Beale, *Structure of the Simple Tissues.* Koster, *Ueber die feinere Structure der Menschlich. Nabelschnur*, ("On the finer structure of the Umbilical Cord,") *Inaug. dissert.* Würzburg, 1868, pp. 16 and 17.

‡ Leydig, Muller's *Archiv*, 1854, p. 316.

§ Gegenbaur, *Monographie der Pteropoden und Heteropoden.* Leipzig, 1855. Max Schultze, Müller's *Archiv*, 1856, p. 314. Leydig, *Vergleichende Histologie.* Kölliker, *Zeitschrift für wissenschaftliche Zoologie*, Band iv., p. 363; and *Würzburger Naturw. Zeitschrift*, Band v., p. 232, 1864.

As long as we consider a given object to belong to this kind of connective tissue from its external appearance alone, and without regard to its chemical and physiological characters, it is difficult to meet the objection that our generalisation is founded on comparatively coarse analogies, which could no longer be maintained were the tissues to be subjected to more accurate chemical and physiological investigation. It may, on the other hand, however, be remarked that a considerable quantity of the connective tissue in the body at a particular stage of its development presents the appearance of gelatinous tissue, and also that in pathological neoplastic formations proceeding from connective tissue the same condition is frequently met with.

b. A very delicate retiform connective tissue, fulfilling the purposes of support and protection, and therefore here first mentioned amongst those possessing similar characters, occurs in the connective tissue of the eye and in the interior of the nervous centres (Neuroglia, Virchow). That this is really a form of connective tissue was first maintained by Max Schultze,* with whom Kölliker,† Virchow,‡ Deiters,§ and others are in accordance. In regard to the particular features presented by this form, we must refer to the special descriptions of the several organs. Hirzel and Frey|| consider they have met the same tissue in the hybernating glands of some mammals.

c. A remarkable form of connective tissue occurs in the supporting and investing reticulum of the glands of the lymphatic system and allied organs in connection with their blood capillaries, and around the fasciculi of fibrillar connective tissue.

In the lymph glands and analogous structures—such as the glands of Peyer, the solitary glands of the intestine, the mucous membrane itself of the alimentary canal, the tonsils, the follicles at the root of the tongue, the trachoma glands of the

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* *De Retinæ Structura Penitiori*, Bonn, 1859. *Archiv für Mikroskop. Anatomie*, Band ii., p. 261.

† *Gewebelehre*. Leipzig, 1867, p. 266.

‡ *Die Krankhaften Geschwülste*, Band ii., p. 128.

§ *Untersuchungen über Gehirn und Rückenmark herausgegeben von* Max Schultze. Braunschweig, 1865, p. 27.

|| Frey, *Histologie und Histochemie*, Leipzig, 1867, p. 233; *und Zeitschrift für wissenschaftliche Zoologie*, Band xii., p. 165.

conjunctiva, the tissue of the conjunctiva itself, and the nasal portion of the pharynx in man—this retiform tissue has been accurately described by Billroth,* Eckhard,† Heidenhain,‡ His § Frey, || Henle,¶ Stieda,** and Luschka.†† The meshes of the network are in all these instances filled with cells resembling those of the lymph in various stages of development. The network and the lymphoid cellular elements have been collectively designated adenoid tissue by His, and cytogenous connective tissue by Kölliker. The trabeculæ of the reticulum may be observed also to traverse the larger cavities of these glandular structures.

In the fresh condition, the reticulum is soft and easily torn. It can only be exhibited in its integrity by carefully brushing fine sections of the hardened tissue with a camel-hair pencil (His), by which means the adhering lymphoid cells can be removed. A delicate network remains behind, composed of nucleated cells which enclose rounded or polygonal areolæ. The trabeculæ of this network proceed from a substance surrounding, and somewhat thicker than the nucleus, which may be regarded as the body of one of the stellate cells from which the trabeculæ are derived. The trabeculæ to which such a cell may be referred as a nodal point, or common point of union, are either simple, and join with similar processes given off from neighbouring cells, or first give off a series of still finer trabeculæ, which then communicate with each other.

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* Müller's *Archiv*, 1857, p. 88, v. *Beiträge zur Pathologischen Histologie*, "Essays on Pathological Histology." Berlin, 1858, p. 126. Virchow's *Archiv*, Band xx., p. 409; and Band xxiii., p. 457. *Zeitschrift für wissenschaftliche Zoologie*, Band xi., p. 325.

† *De glandularum Lymphaticarum Structura.* Berlin, 1858.

‡ Reichert and Du Bois' *Archiv*, 1859, p. 460.

§ *Zeitschrift für wissenschaftliche Zoologie*, Band x., p. 333, v. Band xi., p. 416.

|| *Untersuchungen über die Lymphdrüsen des Menschen und der Saügethiere*, "Researches on the Lymphatic Glands of Man and Mammals." Leipzig, 1861. *Zeitschrift für wissenschaftliche Zoologie*, Band xii., p. 336, and Band xiii., pp. 1 and 28.

¶ *Handbuch der Systematische Anatomie des Menschen*, Band ii., p. 702.

** *Archiv für Mikroskopische Anatomie*, Band iii., p. 360.

†† *Archiv für Mikroskopische Anatomie*, Band iv., p. 1.

The reticulum of the lymphoid organs contains not only cells in its areolæ, but also supports blood-vessels, and the trabeculæ unite upon the external surface of the vessels to form a kind of Tunica adventitia. And hence in the capillaries, this layer was designated by His the Adventitia capillaris. The trabeculæ of the latter must not be confounded with the processes given off from the wall of the vessel itself, which, as they develop, present in the part lying at some distance from the artery, the appearance of a solid trabecula, but which gradually become hollow as they approximate the artery to which they are attached.

The reticulum does not, in all instances, nor in all parts of the organs above named, present the characters of such a network as we have described. When developed to a greater extent, it passes into a network of non-nucleated trabeculæ* which are of a far more rigid nature, and often appear considerably expanded. A trellis-work of this kind may, from its resistance to acids, easily be mistaken for the elastic fibrous networks we shall hereafter describe, and which have a similar plexiform arrangement. But as the latter are distinguished from the fibrillar connective tissue by the circumstance that the connective tissue fibres are never branched and never form networks, though their fibrous bundles frequently present a net-like arrangement; so is this also distinguished from the elastic fibre networks by the circumstance that, unlike these, it is incapable of resisting the action of a solution of soda. It has been previously stated, that reticula, similar to those found in the lymphatic glands, are found also in other places.

A wide-meshed network of trabeculæ is found constituting a kind of investing layer, winding around the bundles of the fibrillar connective tissue hereafter to be described. In consequence of the appearances to which this gives rise, when the fasciculi in question swell up under the influence of acetic acid, it has led some to admit the presence of a structureless sheath surrounding each fasciculus. I† have myself depicted

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* Henle, *Zeitschrift für Rationelle Medicin*, Band viii., 3 R., p. 201. Eckhard, *loc. cit.*

‡ *Wiener Sitzungsberichte*, Band xxx., p. 71, fig. 12.

and given a description of the spiral trabeculæ found in the skin of the ox. Kölliker,* however, still describes these spiral fibres running around the bundles of the pia mater of the fœtus and recently born animals as a nucleated cell reticulum.

A very delicate investing reticulum developed from nucleated cells (perivascular plexus) has recently been described by Iwanoff† in the vessels of the vitreous humour in the frog. He has also pointed out the distinctions which exist between the trabeculæ of the reticulum and the processes of the vessels.

d. A coarser connective tissue network, with large meshes, composed of broad and stiff trabeculæ, forming a firm homogeneous mass, occurs in the Ligamentum pectinatum iridis of

Fig. 1.

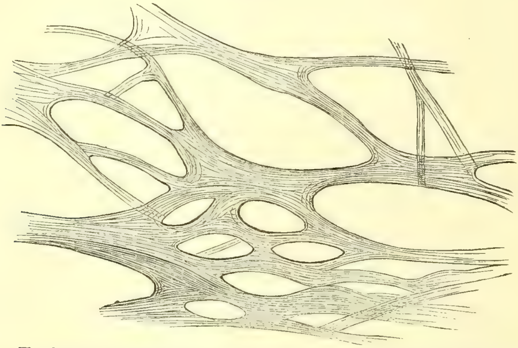

Fig. 1. Trabeculæ from the Ligamentum pectinatum iridis of man.

man. These trabeculæ exhibit an indistinct, interrupted, and not very regular longitudinal striation (fig. 1). Max Schultze has well compared them with the anastomosing fibrous cords of the gelatinous substance composing the Medusæ.‡ The statement made by Haase,§ that the Ligamentum pectinatum of man really consists of the fibrillar form of connective tissue, is erroneous.

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* *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 146; *und Gewebelehre.* Leipzig, 1867, p. 79, fig. 36.

† *Centralblatt für die Medicinische Wissenschaften*, 1868, No. 9.

‡ Müller's *Archiv*, 1856, p. 319, fig. 7.

§ *Archiv für Ophthalmologie*, Band xiv., p. 48, *et seq.*

On the other hand, the Ligamentum pectinatum of animals (ox sheep, pig), differs from that of man in being composed of connective tissue, with which many elastic fibres are intermingled. The gradual modification the trabeculæ of the Ligamentum pectinatum undergo at the point where they become continuous with the membrane of Descemet in man, is worthy of particular remark, as it can be clearly seen to occur, especially in new-born infants. The trabeculæ widen out; the meshes diminish in diameter, and, near the membrane of the vitreous humour, only present small interstices. In human embryoes of about the fifth month, the Ligamentum pectinatum can be still seen to be composed of cells which give off broad processes, communicating with one another in the same way that the trabeculæ do at a later period. In some of these cells the nucleus, which subsequently vanishes, is already small, dull in appearance, and ill-defined, though in others it is still granular and distinct. The latter features are well brought out in preparations coloured with carmine. A great number of beautifully defined stellate cells occupy the interspaces of the trabeculæ of the Ligamentum pectinatum just described.

e. There still remains to be mentioned the connective tissue supporting masses which occur in various places, and are composed of fusiform and stellate cells. The best example we can adduce of this is the connective tissue in the interior of the kidneys.* This does not present any proper reticulum comparable to that of the previously described forms. In sections of the organ from which the gland tubes have been removed by pencilling, a connective tissue meshwork can indeed be exhibited; but it may also be seen that its trabeculæ form a laminated mass, supporting or investing the tubuli of the gland, in which fusiform and stellate cells lie closely congregated together. Boll† has recently described and represented

* *A Beer, die Bindesubstanz der menschlichen Niere*, etc., "The Connective Tissue of the Human Kidney," etc. Berlin, 1859. Isaac's *Recherches sur la Structure et la Physiologie du Rein, Journal de la Physiologie*, T. i. Paris, 1858, p. 577. Kölliker, *Handbuch der Gewebelehre*. Leipzig, 1866, p. 509.

† *Archiv für Mikroskopische Anatomie*, Band iv., p. 146, T. i.

a plexiform connective tissue, consisting of a simple layer of cells united into a plexus, investing the acini of the salivary and lachrymal glands.

An investing layer of fusiform cells constituting a perineurium may be found also on the peripheric branches of nerves, especially amongst the Batrachia.

A similar covering is also found in the excretory ducts of the mammary glands and elsewhere.

The forms of connective tissue hitherto described are distinct from the fibrillar connective tissue which is so frequently found in the adult organism. In this, the connective tissue fibrils, which are so well characterised by their yielding gelatine on boiling, by their unbranched course, their smooth edges, and equal thickness, constitute the essential morphological constituent. It must be admitted, however, that in certain cases transitional forms occur between the fibrillar and the above-mentioned forms of connective tissue. These may be met with in many places, but clearly do not hinder us from admitting that in other places a distinction may be drawn between the two in accordance with the facts already given. Otherwise, the difficulty may easily arise that was frequently observable in the old discussion as to whether the structures under examination should be regarded as connective or as elastic tissue.

FIBRILLAR CONNECTIVE TISSUE.—This is the most widely distributed form that is found amongst the Vertebrata; but it has not been clearly proved whether it occurs amongst the Invertebrata. The connective tissue which is most similar to the fibrillar connective tissue of Vertebrata is that described by Leydig in the Cephalopods.* According to the same inquirer,† a fibrillar connective tissue, very similar to fibrous connective tissue, occurs also in the Echinodermata. Reichert described as belonging to connective tissue, certain tissues found in Arthropods, Molluscs, and Vermes. No evidence, however, is furnished, that these tissues are gelatine yielding. Several of

* Muller's *Archiv*, 1854, pp. 303 and 310.
† *Loc. cit.*

them probably consist rather of Chitin. Schlossberger* obtained no gelatine from the claws of crabs.

Originally, fibrillar connective tissue, as already mentioned, was the only form to which the term connective tissue was applied. The morphological constituents which can be demonstrated in it, are fibres and cells of various kinds. These elements are only here and there in direct contact with each other; elsewhere the intervening spaces are occupied with a material of variable consistence.

In the fibrillar connective tissue of adult animals a certain kind of the fibrous elementary form constitutes so large a proportion of the old tissue that it exclusively occupied the attention of the earlier investigators. This is composed of the

Fig. 2.

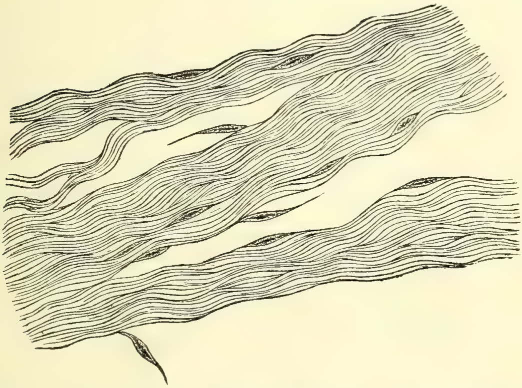

Fig. 2. Tendon of man, showing fibrils and fusiform cells.

already frequently mentioned gelatine-yielding fibril. The simplest preparation, the mere teasing out with needles of a small portion of fibrillar connective tissue, shows that it may be split into skein-like portions of various breadth.

The lateral borders of these cords present straight or more or less sinuous outlines; and with strong magnifying powers fine striæ may be observed lying in close contiguity to one

* *Chemie der Gewebe. Leipzig und Heidelberg*, 1856, p. 300.

another, and following accurately, in a longitudinal direction, the contour of the cord. In thin transparent membranes, as for example, in the mesentery, or in the arachnoid, these fasciculi of the connective tissue may be immediately recognised without any preparation. If such longitudinally striated cords be further broken up, we may easily convince ourselves that in accordance with the longitudinal striation they exhibit (fig. 2), they may be split into fine smooth fibres, running for considerable distances without apparently giving off any branches. The diameter of these fibres is very small, varying from 0·0006 to 0·002 millimeters. These fibres are the fibrillæ of the connective tissue; and when examined by means of the polarizing microscope, the fibrils and the fasciculi they form prove to be doubly refractile.* The axis lies in the longitudinal direction of the fibrils, and they behave as positive uniaxial crystals.† They cannot, however, be isolated from the connective tissue by simple mechanical means. We possess, however, in solutions of lime and baryta, fluids which, if they have acted for some time upon connective tissue, loosen the adhesion of the fibres to one another to so great an extent that nothing further is required to obtain the detached fasciculi and even completely isolated fibres for microscopical investigation. The lime-water in which connective tissue, freed as far as possible from extraneous substances (*e.g.*, clean tendon), has undergone this loosening of its cohesion, contains a substance which can be precipitated from it by means of acetic acid in the form of white granules, which subsequently form flocculi. This reaction still occurs, even if the connective tissue, before being placed in the lime-water, has had all the albuminous substances soluble in water, as far as possible withdrawn from it. The substance taken up by the lime-water, and capable of being again precipitated from it, agrees in its reactions with

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* Erlach, Müller's *Archiv*, 1847, p. 322.

† W. Müller, *Zeitschrift für Rationelle Medicin*, 3 R., Band x., p. 173. See also Valentin, *Untersuchung der Pflanzen, und Thiergewebe im polarisirten Lichte*, p. 265, "Researches on the Tissues of Plants and Animals in Polarised Light;" and Mattenheimer, Reichert and Du Bois' *Archiv*, 1860, p. 354.

Mucin.* On account of the mechanical alteration which the connective tissue fibrils undergo by this procedure, it may reasonably be admitted that a solution has taken place of a cementing substance occupying the interspaces between, and binding together, the fibrous elements.† Wherever the fasciculi of the connective tissue appear separated to a considerable distance from one another, an intervening material of this kind may be directly observed. Statements in accordance with this were first made by Schwann, and subsequently by Henle, the meshes of the arachnoid being particularly alluded to by the last-named author.‡

Kühne § demonstrates the possession of quite definite mechanical peculiarities by the homogeneous substance intervening between the muscles of the frog which only contains scattered fibrils. A separation of connective tissue into fibrils can also be attained through the chemical action of permanganate of potash. || Connective tissue, when acted on by permanganate of potash, becomes stained of a brown colour; and if it be then treated with boiling nitric acid and ammonia, it no longer assumes a yellow colour. Connective tissue that has been well washed,¶ furnishes only feeble indications of the xantho-proteinic acid reaction.** The same occurs with tendons that have undergone calcification. It thus appears that it is not the collagenous substance which causes all insufficiently purified connective tissue to become stained yellow with these reagents.†† The fibrils of the connective tissue, and the fasciculi which they form, undergo a peculiar change at a high temperature. When placed in boiling water, they rapidly contract, becoming shorter but much thicker than in the fresh condition, and at the same

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* Rollett, *Sitzungsberichte der Wiener Akademie*, Band xxxix., p. 308. Eichwald, *Annalen der Chemie und Pharmacie*, Band cxxxiv., p. 177.

† Rollett, *Sitzungsberichte der Wiener Akademie*, Band xxx., p. 43.

‡ Henle, *Allgemeine Anatomie*, p. 349.

§ Kühne, *Lehrbuch der Physiologischen Chemie*. Leipzig, 1866, p. 359.

|| Rollett, *Sitzungsberichte der Wiener Akademie*, Band xxxiii., p. 519, *et seq.*

¶ Rollett, *loc. cit.*, Band xxxiii., p. 523.

** Donders, *Holländische Beiträge*, Band i., 1848, p. 67.

†† Paulsen, *Observationes Microchemicae*. Mitau, 1849.

time presenting a much more delicate outline. Coincidently the characteristic longitudinal striation of the fasciculi is lost. These, equally with the compact connective tissue in which coarse fasciculi lie in intimate connection with one another, assume the appearance of a homogeneous mass, in which, however, under the microscope, various deposits that scarcely appear in the fresh tissue, or altogether escape notice, are clearly brought into view.

The sudden shrivelling which the fibrils of connective tissue undergo in boiling water, depends on a peculiar molecular metamorphosis of the substance of the fibrils. It is impossible to demonstrate that any imbibition of water occurs. If the connective tissue be exposed to a boiling temperature, whilst at the same time any shortening in the longitudinal direction of the fibres is prevented, the tissue thus heated, when dried, still retains, under the microscope, its fascicular and fibrous character. If small portions of tendon are macerated in water of various temperature, it will be observed that sudden contraction occurs at as low a temperature as between 140° and 158° Fahr. When connective tissue is long subjected to a boiling temperature, or is placed for a shorter time in a Papin's digester, or if, in its natural condition of moisture, it is heated in a test tube to 248° Fahr.,* it dissolves away in the manner already mentioned, and the fibres can in this mode be isolated. The solutions which are obtained usually contain gelatine or "Glutin."

On account of their property of yielding gelatine on boiling, the fibrils and fasciculi of connective tissue are termed collagenous substance. The conversion into gelatine occurs even at 104° Fahr., providing dilute acids have been added; as for example, sulphurous acid,† or 0·1 per cent of sulphuric acid.‡ Founded on these facts, methods have been suggested for the isolation of microscopic structures which do not yield gelatine, but which are imbedded in or surrounded by connec-

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* Rollett, Kühne, *Ueber die peripherischen Endorgane der motorischen Nerven*, p. 6. Leipzig, 1862.

† Ruthay, *Annalen der Chemie und Pharmacie*, Band xli., p. 236.

‡ Kühne, *loc. cit.*, p. 11.

tive tissue. The first effect of the acid, when applied at ordinary temperatures, is that the tissue swells up to a great extent, especially in the direction of the transverse diameter of the fasciculi and fibrils. The latter, which are thus rendered less strongly refractile, become so compressed against one another with their glutinous surfaces, that their contours can no longer be distinguished ; and in the transparent mass, as in boiled connective tissue, new elementary forms now make their appearance. Acetic acid is usually employed to produce this change, and by this means to distinguish the fibrils of connective tissue from those of other fibrous structures.

Several other vegetable acids and diluted mineral acids, especially hydrochloric acid of 0·1 per cent., and similarly diluted nitric acid, act in the same manner as acetic acid.

After treatment with acids, contractions resembling an hourglass frequently occur in the fasciculi of connective tissue, their enlargement appearing to be prevented at certain points by a firmly applied ligature. These are the much-discussed fasciculi of connective tissue surrounded by coiled fibres. The appearance of constrictions was formerly held to be due to spiral fibres winding round the fasciculi, which, on account of their not swelling in acetic acid, were considered to be of an elastic nature.*

At a later period attempts were made in various quarters to support a view first advanced by Reichert,† which attributed the contractions of the swollen bundles to the sheath of the connective tissue being torn in the act of swelling up into looplike portions. The presence of such a sheath covering the fasciculi in the form of a continuous membrane cannot, however, be demonstrated in fresh fasciculi; we may, however, convince ourselves of the presence of coiled fibres forming a plexus around these, the fibres being sometimes finer and sometimes coarser. On the cautious addition of alkalies to connective tissue swollen

* Henle, *Allgemeine Anatomie*, Band cxcv., *Jahresbericht für* 1857, p. 38.

† Reichert, Müller's *Archiv*, 1847. Leydig, *Histologie des Menschen und der Thiere*. Frankfurt, 1857, p. 31. Klopsch, Müller's *Archiv*, 1858, p. 417. Kölliker, *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 140.

by means of acids till neutralization is effected, it may again be made to resume its original appearance; a fact which Henle first adduced against Reichert's view, who especially rested his doctrine upon the absence of apparent structure in the fibrillar connective tissue when acted on by acetic acid, and on the impossibility of splitting connective tissue into fibres otherwise than by mechanical means. The proposition of Reichert is also negatived by the facts already adduced.

In reference to the capability of bringing back the fibrils and bundles to their original condition after having been swollen by immersion in acids, it must be remarked that the experiment must not be too long delayed, since protracted action of acids even at a low temperature, actually effects the solution of the fibrils with formation of gelatine. It is further to be remarked that, in solutions of pure alkalies, connective tissue in the first instance swells up into the form of a transparent jelly, and that at a later period the fibrils undergo complete solution. Concentrated nitric acid, at the commencement of its action, causes the same sudden contraction of the fibres of connective tissue that occurs at temperatures exceeding 140° Fahr. When covered with chloride of calcium or potash, the fasciculi and fibrils become hardened by the withdrawal of water. In solutions of tannin a sufficient quantity of connective tissue soon removes all the acid. Leather thus obtained, especially if the connective tissue have previously been exposed to the action of lime, is better adapted than when hardened by other means, for the preparation of fine sections, to exhibit the arrangement of the fasciculi in compact masses.*

If in such sections the fasciculi, hitherto only considered in the direction of their length, be cut across, the fine transverse sections of the fibrils lying in close contiguity with one another appear in the form of round or somewhat angular dots. This view is, however, far better obtained if the fresh tissue be allowed to freeze on a leaden plate, resting on an iron support, and so imbedded in a freezing mixture that only the upper surface is exposed, the sections being then made on the plate

* Rollett, *Sitzungsberichte der Wiener Akademie*, Band xxx., p. 45, fig 3, Taf. 1.

with a cold knife. Henle and Stadelmann* were the first to see the transverse sections of the fibrils in sections of dry tendon.

Sections made from frozen or dry tendons, when treated with acetic acid, are so acted on that the edges of the divided fasciculi curl up, as a consequence apparently of the rapid swelling that takes place in the direction of their transverse diameter. A peculiar appearance is thus presented, which was first described by Donders,† and more recently by Gerlach,‡ and Machik.§ The involuted edges cross each other in the form of broad bands with transversely striated surfaces and sinuous borders.

The fibrils and fasciculi of fibrils of connective tissue are differently disposed in different instances.‖ The fasciculi may either run parallel to one another, or unite at very acute angles, as in tendons and ligaments ; or the variously sized fasciculi, as they decussate at different angles, may divide and again unite to form a thicker or thinner felt-like layer, through which three sections perpendicular to each other may be so carried as that one may strike all the bundles principally in the longitudinal direction, whilst the other two present fibres running in an oblique and transverse direction. In either of the two latter sections the fasciculi may run chiefly in one or other direction, and thus transitional forms may originate, passing into a parallel arrangement. The modes of arrangement above described are found principally in the skin and other membranes composed of connective tissue.

A peculiar arrangement of the fasciculi occurs in the serous membranes, and is most beautifully displayed in the peritoneum of man (fig. 3) and many mammals. The fasciculi of fibrils coursing in this thin membrane, by their frequent division and

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* *Sectiones transversæ*, etc., *Diss. inaug.*, 1844 ; Henle's *Jahresbericht*, 1844, p. 15.

† *Holländische Beiträge*, Band i., p. 258.

‡ *Handbuch der Gewebelehre*, Mainz, 1850, p. 110, fig. 42.

§ *Sitzungsberichte der Wiener Akademie*, Band xxxiv., p. 91.

‖ Bruch, *Zeitschrift für Rationelle Medicin*, Band vii., pp. 378 and 379. Leydig, *Histologie des Menschen und der Thiere*. Frankfurt, p. 79. Rollett, *Sitzungsberichte der Wiener Akademie*, Band xxx., p. 45, *et seq.*

reunion, have larger or smaller interstices between them, so that the whole membrane presents a gauzy appearance. A very important character to be noticed here is, that the borders of the interstices contain loops of fibrils which appear to round off the angles.

Fig. 3.

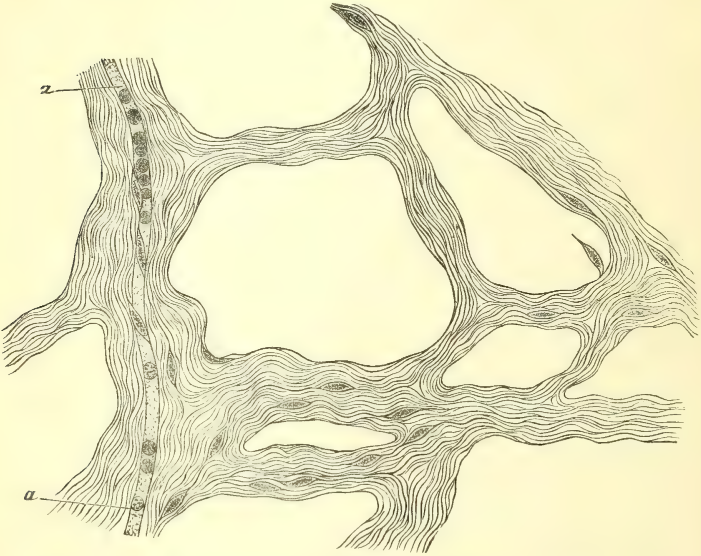

Fig. 3. Fibrillar connective tissue from Peritoneum of man. *a a*, a blood-vessel.

The foregoing arrangement has been described as a special form of connective tissue, under the name of the retiform,* or areolar connective tissue.† These expressions, however, refer only to the peculiar appearances presented under the microscope.

Another mode of arrangement exhibited by the fasciculi of connective tissue is that in which, of three sections made perpendicularly to one another, none of the fibrous bundles run chiefly longitudinally or transversely, but each section presents

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* Kölliker, *Gewebelehre.* Leipzig, 1867, p. 74.

† Hassall, *Mikroskopische Anatomie,* translated by Kohlschütter. Leipzig, 1852, p. 232, Taf. 35, fig. 7.

bundles running in the most various directions. This form occurs, but not exclusively, in the interstitial connective tissue of various organs, as well as in the amorphous connective tissue of Henle,* whilst the kinds previously described preponderate in the formed connective tissue of Henle. Henle himself, however, has not attempted to draw a very sharp line of distinction between them.

Differences between the connective tissue of different organs not only occur in regard to the arrangement of the fasciculi, as we have already remarked, but the fasciculi themselves show varieties, so that in certain organs the fine fibrils appear in all transverse sections of a fasciculus arranged parallel to one another, and at equal and very small distances, resembling the straight or slightly sinuous edge of a fasciculus, whilst in other instances the fibrils are collected into smaller fasciculi, the borders of which present very close undulations, and which are more loosely arranged. On this account, when treated with lime and baryta-water, the first kind of fasciculi immediately splits into fibrils, whilst the second divides in the first instance into sections, and these again break up into fibrils.

I have already elsewhere observed† that these differences are most clearly discernible on making a comparative examination of the sclerotic and conjunctiva of the same eye.

Fasciculi of the former kind occur in the tissues that were formerly called fibrous. Fasciculi of the latter kind in ordinary connective tissue.

A few remarks may here be made in regard to the lacunæ or interstices of connective tissue.

It is impossible for any one who has carefully examined the structure of this tissue to doubt that interfibrillar fissures occur in it. It is also extremely easy to perceive that the collagenous substance is not in equally intimate contact in all parts of a given portion, or, in other words, that it does not everywhere cohere with equal firmness. The varieties in the arrangement of the fibrils and of the fasciculi, and the results of the disintegration which occurs with lime and baryta-water also clearly prove this, especially in those forms of connective tissue where

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* *Allgemeine Anatomie*, p. 354.

† *Loc. cit.*, p. 58.

the above-mentioned coiled or ring-like arrangement of fibres around the fasciculi is absent.

It cannot therefore be maintained that the fibrils and fasciculi swim in a fluid equally distributed amongst them, as Engelmann* holds to be the case in the cornea, nor can we admit with His† that the mucous or mucoid substance, nor the above-mentioned cementing material, is quite equally distributed between the fibrils and fasciculi. The experiments made by Von Wittich,‡ in which he endeavoured to demonstrate experimentally the existence of the plasmatic canal system of Virchow, by allowing tendons to absorb particles of indigo through the action of capillarity, and in which he found a finely divided blue precipitate in the tendons, do indeed speak in favour of this view. It is impossible, however, to prove by such means that the passages between the firmly united fasciculi and fibrils can be represented in the form of a canal system communicating with the origins of the lymphatic capillaries, analogous to that described by Von Recklinghausen§ under the name of serous canals, from the appearances presented after treatment with nitrate of silver. These questions will be discussed in the section on the lymphatic system. It must be acknowledged, however, in regard to the migrating cells of this form of tissue considered generally that they cannot enter it at any point indiscriminately, but only through determinate passages, resulting not only from the impermeability of the collagenous substance, but also from the unequal distribution of the firmer cementing substance.

The mode in which the cells of the fibrillar tissue can best be represented and investigated has already been given. If we have pursued this plan with tissue in as fresh a condition as possible, it will always be found that fibrils and cells are coincidently brought into view (figs. 2 and 3). It may here further

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* *Ueber die Hornhaut des Auges,* "On the Cornea." Leipzig, 1867, p. 6.

† *Die Häute und Höhlen des Körpers,* "The Membranes and Cavities of the Body." Basel, 1865, p. 23.

‡ Virchow's *Archiv*, Band ix., p. 187.

§ *Die Lymphgefässe und ihre Beziehung zum Bindegewebe,* "The Lymph Vessels, and their relations to Connective Tissue." Berlin, 1862.

be mentioned that very beautiful preparations may be obtained in dense connective tissue by the aid of chloride of gold, after the action of which the cells appear red or bluish red, whilst the fibrous material remains uncoloured.* Formerly, acetic acid was frequently employed to bring the cells of connective tissue into view; but on account of the changes which this reagent induces in the cells, and the circumstance that the true disposition of the fibrils and fasciculi disappear under its influence, the modes of treatment above recommended will be found to be more appropriate.

The subjection of the tissue to a boiling temperature was in like manner formerly recommended;† but, as we now know, this method leads to illusory appearances of the stellate cells brought into view on making transverse section of tendons.‡ It is also apt to produce erroneous impressions in the case of other organs composed of connective tissue, from the circumstance that the contracted closely compressed fasciculi, where they lie in juxta-position in the transverse section, present three or four-sided fissures with incurved sides between them.

Besides the cells, sharply defined fibres become apparent in connective tissue either after treatment with acids, or on boiling, as we shall presently describe. Where, however, it is desired to obtain a rapid general view of the disposition of these parts, the last-mentioned method can alone be employed.

THE ELASTIC FIBRES.—These fibres, which are apparent in all forms of connective tissue that have been rendered transparent by treatment with acetic acid or by boiling, are sharply defined, and present smooth edges. In boiled connective tissue they are distinguished by their spiral or coiled course, but in connective tissue swollen by immersion in acid they pursue a somewhat straighter course. These fibres are distinguished

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* Cohnheim, *Archiv für Pathologische Anatomie*, Band xxxviii., p. 352.

† Henle, *Jahresbericht*, 1850, p. 40; and Virchow, *Würzburger Verhandlungen*, Band ii., p. 154.

‡ Henle, *Jahresbericht*, 1851, p. 23. Reichert, Müller's *Archiv*, 1854, p. 38. Bruch, *Zeitschrift für wissenschaftliche Zoologie*, Band vi., p. 474. Rollett, *loc. cit.*, Band xxx., p. 69.

from those of the connective tissue, not only by the resistance which they offer to the above-mentioned agents, but also by the circumstance that they present a remarkable tendency to branch and form networks. They are sometimes only sparingly present, and then usually exhibit the form of cylindrical delicate fibrils of about the same size as those of the connective tissue—slightly branched, and forming long large meshes, as in the tendons of man; or, on the other hand, they may be present in greater numbers, may branch repeatedly, and, being connected by frequent anastomoses, form a fine delicate plexus, as on the surface of many serous and mucous membranes. The several fibres may also coalesce to form one of considerable thickness; they may also expand in the form of flattened trabeculæ, which combine with similar or still finer fibres proceeding from the branches of the trabeculæ, to form a very characteristic plexus, as in the cutis and the lungs. In several places, as, for instance, in the ligamentum nuchæ of animals, in the ligamenta subflava of the vertebral column, and in the elastic tissue of the arteries, the elastic fibres exist in such quantity that they are commonly regarded as forming an independent elastic tissue or membrane. The fibres here are for the most part thick, and branch and communicate at more or less acute angles, so that only narrow and elongated, or small round or oval meshes, lie between them. The trabeculæ often appear very much expanded, or become fused together into elastic plates or membranes, which are perforated by sharply defined foramina constituting the so-called fenestrated membrane of the arterial tunics.

The elastic fibres undergo no change from exposure to the action of either dilute or concentrated acetic acid, and they resist for a very long period, at ordinary temperature, the action both of potash and soda. The latter forms one of the best means of bringing them into view. Concentrated sulphuric acid makes the elastic fibres clearer without immediately causing them to swell up, and its action requires to be continued for many days before the fibres swell and begin to dissolve. The elastic fibres do not dissolve on boiling, at least in the time requisite to convert the collagen of connective tissue into gelatine; and if connective tissue and albuminoid substances have been removed from the specimen, as, for instance, from the ligamentum nuchæ,

by means of solution of potash, no gelatine, in the ordinary sense of the word, can be obtained. It must be admitted, however, that the elastic fibres themselves undergo solution on continuous boiling,* or on exposure to a temperature of 320° Fahr. for thirty hours. By these means, however, only a non-gelatinising brownish fluid can be obtained, smelling of glue, and precipitable by tannic acid.

Moreover, if connective tissue be converted into gelatine by digestion with acids, at 104° Fahr., the elastic fibres remain unaffected.† The elastic fibres are reddened with Millon's reagent, and give the xantho-proteinic acid reaction. The ligamentum nuchæ, after being purified by successive treatment with alcohol, ether, boiling water, acetic acid, and alkalies, has been described and analysed by W. Müller‡ under the name of Elastin.

In the elastic fibres of the skin and of the subserous layers of the peritoneum, and of the chordæ tendineæ of the dog, Von Recklinghausen§ saw, after treatment with nitrate of silver, a black precipitate occur here and there in the interior of the fibres, and is hence inclined to regard them as hollow. This appearance does not occur in the fibres of the ligamentum nuchæ, nor in those of the elastic coat of the vessels. Frey‖ believed that he had witnessed a precipitation of carmine granules in the interior of many elastic fibres after maceration in a solution of carmine and ammonia, and subsequent neutralization with acetic acid; but he is doubtful whether the question of the tubular nature of the fibres can be thus decided. Von Wittich¶ obtained no precipitate in the elastic fibres of the ligamentum nuchæ in his experiments with indigo. There is certainly no indication of an internal cavity presented on the examination of the broad transverse sections of the elastic fibres of this ligament.

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* Eulenburg, *De tela Elastica*, Berlin, 1836; and J. Müller, Poggendorf's *Annalen*, 1836, Band xxxviii., p. 311.

† Kühne, *Physiologische Chemie*. Leipzig, 1866, p. 356.

‡ *Zeitschrift für Rationelle Medicin*, Band x., 3 R., p. 173.

§ *Die Lymphgefässe*, etc., p. 59.

‖ *Histologie und Histochemie*. Leipzig, 1867, p. 247.

¶ *Archiv für Pathologische Anatomie*, Band x., p. 187.

DISTRIBUTION OF THE FIBRILLAR CONNECTIVE TISSUE IN MAN.—In regard to this point, the parts that consist of fibrillar connective tissue in man are the ligaments of the skeleton, the periosteum, and perichondrium; the aponeuroses, fasciæ, and tendons; the fibrous membranes, the stroma of the serous membranes, of the majority of mucous membranes, and of the skin; and the subserous, subcutaneous, and submucous connective tissues: it occurs also in the tunics of the vessels, especially in the tunica adventitia and in the endocardium, in the vascular membranes of the eye, and of the central nervous apparatus, and as interstitial connective tissue in most organs.

DEVELOPMENT OF CONNECTIVE TISSUE.—The question of the development of fibrillar connective tissue is one of the most difficult in the whole range of histological inquiry. After Henle* had opposed the view of Schwann,† that the cells becoming greatly elongated split into the fasciculi of fibrils, the view of the latter constantly gained ground, that an originally homogeneous substance, containing certain constituents, distributed through it subsequently split into fasciculi and fibrils. But the significance attached to the various forms and material here met with by various authors was very different. According to the view of Reichert,‡ the homogeneous substance which subsequently becomes converted into the fasciculi and fibrils, proceeds from the coalescence of cell membranes with an intercellular substance; the fasciculi and fibrils are only the optical expression of a duplicature of this substance, whilst the cells, with their nuclei, or with the exception only of their nuclei, undergo atrophy. According to another explanation, it is not the blastema existing between the nuclei that undergoes conversion into a fibrillar tissue, but the formed elements between which this is so abundant as an intercellular substance, and which are the fusiform cells demonstrated by Schwann in embryonic connective tissue. The latter, again, ac-

* *Allgemeine Anatomie*, p. 379.

† *Mikroskopische Untersuchungen über die Uebereinstimmung*, etc. Berlin, 1839, p. 133, *et seq.*

‡ *Beiträge zu vergleichende Anatomie*, etc., p. 108.

cording to Virchow,* Donders,† and Kölliker,‡ take no share in the fibrillation of the tissue, but persist in a somewhat atrophied condition as cells (Virchow, Kölliker), or become converted into a plasmatic canal system (Virchow), or, lastly, pass through transitional forms into a plexus of elastic fibres (Donders).

Max Schultze§ and Beale,|| as has been already stated, and with whom many others agree, consider the matrix which is gradually assuming a fibrillar form, to be the protoplasm of membraneless embryonic cells which have fused with one another, and the remains of which, after the formation of the fibrils, are represented by the nuclei with a little unaltered protoplasm around them, constituting the so-called connective tissue corpuscles.

Very recently, Kusnetzoff¶ and Obersteiner** have maintained that the fibrils of connective tissue originate immediately from the outgrowth of undivided or branched processes of the cells.

In opposition to these various views we must first fix our attention on those definite forms with which we meet in following out the development of connective tissue through as many stages as possible.

And, in the first place, it must be remarked that the tendons and other more dense connective tissue structures, do not furnish the most appropriate objects for examination. Better specimens are obtained from the thin laminæ of serous membranes which were used by Henle and Baur. The peritoneum of the embryo of man and other animals, preserved in Müller's fluid, constitutes an exceptionally good object for examination.

After removal of the epithelium it will there be seen that the superficial layer consists of roundish or somewhat elongated closely compressed cells. In the embryo of a sheep, measuring

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* *Loc. cit.*

† *Loc. cit.*, Band iii., p. 348.

‡ *Neue Untersuchungen über die Entwickelung des Bindegewebes.* Wurzburg, 1861. *Gewebelehre.* Leipzig, 1867, p. 76.

§ Reichert and Du Bois' *Archiv*, 1861, p. 13.

|| *Loc. cit.*

¶ *Sitzungsberichte der Wiener Akademie*, Band lvi., p. 162.

** *Idem*, p. 251.

an inch and a half, these cells are on the average 0·0256 in length, and 0·0096 in breadth; their nuclei are round or slightly oval; they have a granular aspect, but the granules possess no peculiar brilliancy, and the whole nucleus is not distinguished from the surrounding protoplasm by any very sharp line of demarcation. The protoplasm of the cell appears faintly clouded without distinct granulation. Where these cells lie in close contiguity, their contour lines either altogether disappear or are but feebly marked. The cells may be obtained

Fig. 4.

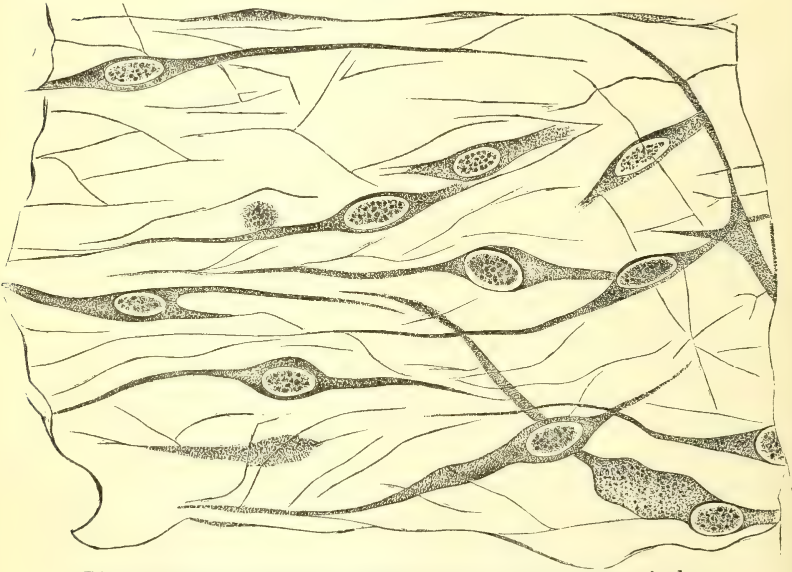

Fig. 4. From the decidua of the embryo of a sheep three inches in length.

in an isolated condition at the edges of the preparation, or on slightly breaking the specimen up with needles.

When these appearances are visible, and they may be rendered much more distinct by staining with carmine, we may easily imagine we have a blastema containing nuclei or coalesced masses of protoplasm, from the cleavage of which the fibrils originate, before us; but this period is still very remote from that at which fibrils make their appearance in the peritoneum. The

appearances above described pass immediately into the following.

The nuclei, which in the first instance are ill defined, become vesicular, with distinct double contours at their margins; they are transparent, but contain in their interior a mass of coarse granules elongated in the direction of the longer axis. The cells become attenuated, and assume an elongated spindle shape (fig. 4). The processes are here and there knotted, branch sparingly, and are frequently connected with one another by their extremities. Two enlargements containing nuclei are often only connected together by a short bridge of protoplasm, and with their processes present the appearance of a bi-nucleated double fusiform mass. Fusiform cells divided transversely may also in some instances, though rarely, be seen. These long and beautiful fusiform cells appear to be widely separated from one another by a clear substance, in which, at an early period, nothing more may be perceived than short interrupted sinuous lines. It is very remarkable that between the above-described elongated cells other round cells are scattered; these exhibit a granular appearance, and one or more round nuclei resembling those of the amœboid cells. The formation of these structures may be well followed in the above-mentioned embryoes of sheep of from an inch and a half to two inches in length, and here most beautiful examples of the fusiform cells of embryonic connective tissue described by Schwann and Virchow may also be seen. Such fusiform cells occur also abundantly in the peritoneum of older embryoes, but during their intra-uterine life they pass their prime. Their processes in particular become attenuated, though they still remain very long, and it requires considerable trouble to follow them out to their termination. It is at this period that the looped smooth unbranched fibrils first appear in small numbers and scattered in the clear matrix between the cells. These, crossing the cell processes at various angles, may be followed over an entire series of fusiform cells; in many instances, however, they attach themselves for a short distance to the long axis of the fusiform cells, and appearances are then produced which may easily lead to the idea of a connection between the fibrils and the cells. But there are many other appearances by

which we may convince ourselves that such a connection between the very finely pointed cell processes and the equally fine fibrils does not exist. By commencing at the cells, and using proper precautions, their long processes may be followed quite to their extremity with a No. 10 immersion lens of Hartnack; on the other hand, the individual fibrils may be equally well followed throughout the entire preparation, and over all the cells continuously, in the form of smooth, slightly sinuous, but never thickened threads. The substance of the

Fig. 5.

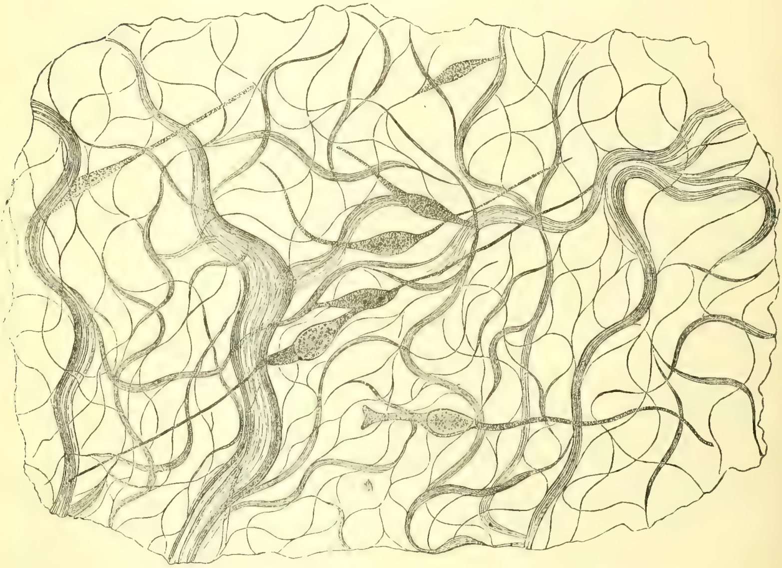

Fig. 5. From the peritoneum of a human embryo of the age of five months.

cell processes becomes somewhat more strongly coloured with carmine than the fibrils; their border, however, has not so smooth an appearance, but exhibits very fine irregularities, and is at short distances slightly varicose and somewhat angularly bent.

At the time when the fibrillæ make their appearance the connective tissue of the peritoneum forms a continuous lamella, remaining in this condition until, in addition to several looped

fibrils, fasciculi have also become developed. The peritoneum of a human embryo at the fifth month permits a very clear view to be obtained of the fascicular fibrils and fine elongated fusiform cells (fig. 5).

At a later period, however, there appear in man and certain animals—for example, in the dog, but not in the sheep—larger or smaller sharply defined foramina.* In human infants these are much less numerous and much smaller than in adults, and the fine striæ of the surrounding fibrils may be here observed running close to the margin of each foramen.

If the process of development be further followed, as I have done in the peritoneum of a child of one year old, and from thence up to the eleventh year, we may observe that the number of the foramina in the membrane undergoes continuous increase, and the fasciculi and bundles of fibrils augment in thickness, which may be particularly well seen in the fibres surrounding the foramina. It certainly cannot be observed during this growth of the membrane that the fibrils originate from the processes of the cells.

If we pass from the examination of the peritoneum to the tendons of embryoes, treated in a similar manner, much caution must be used in drawing conclusions respecting the appearances presented.

In young embryoes, closely compressed roundish formative cells may be found at an early period, containing as yet only imperfectly differentiated nuclei. Such cells become, to some extent, elongated in the direction of the long axis of the tendon, and their margins are not very well defined. The isolated cells present the appearance of delicate flocculi in carmine preparations, with the deeply reddened nucleus in their centre. These cells subsequently increase in point of length, as do also their nuclei, the latter becoming at the same time more sharply defined, clear at their margins, and presenting an elongated mass of granules in their interior. The elongated cells appear to be composed of a more strongly refractile substance than the primitive cells, and are capable of being more easily isolated. A clear, smooth intervening substance similar to that which

* See Bruch, *Zeitschrift für Rationelle Medicin*, Band viii., fig. 1.

precedes the conversion of connective tissue into plexuses of fibrils, is not here visible; on the contrary, we constantly meet with fine, smooth, completely homogeneous and transparent fibrils, which at first are only few in number, but are subsequently more numerous, lying between the cells which have then become elongated, better defined, and more attenuated. The fibrils can be easily isolated by teasing out the tissue, providing the cells have not become very much elongated, and they may also frequently be followed without interruption over the whole extent of the portion of tendon under observation. If the cells have become elongated, and they undergo lengthening both in an absolute sense, as well as relatively to their breadth—their breadth, indeed, becoming absolutely less—the number of the fibrils undergoes a considerable increase. These, again, may be followed uninterruptedly through the entire tendon, as well as over a whole series of cells. Lastly, amongst a large number of recently formed fibrils more attenuated elongated fusiform bodies are found, the extremities of which present long and fine points. These bodies can be easily isolated, although their fine extremities adhere intimately to the fibrils. With a proper degree of care we may convince ourselves of their essential independency, and may follow many of the fibrils from one end of the tendon to the other, as smooth homogeneous threads without any indication of nodal points. This, as has been above stated, is only possible whilst the cells are still proportionately broad and short. The further process of development consists in the great increase in the number of the fibrils, in the separation of the cells from one another, and in their becoming gradually more and more completely atrophied. In recently born children, and in adults alike, the atrophied fusiform cells, as appears from what has already been stated, present the same aspect as at all periods of embryonic life, and we never in any instance find a cell intercalated in the course of a fibril.

From these observations it follows that, in the foregoing cases, any development of the fibrils by the growth of cell processes must be regarded as questionable.

The fibrils appear to be formed simultaneously for considerable portions of their length. The cells contained in the

embryonic mass which is destined to form connective tissue, either all increase in the process of development to fusiform cells of considerable length, at the same time separating from one another in such a mode that at first a small, but subsequently gradually increasing number of fibrils appear between them, as in the tendons, or that at first a transparent, interruptedly striated substance occurs in great quantity, in which the fibrils become apparent at a later period, as in the peritoneum. This is what, in brief, I believe every one may convince himself of.

As regards the significance of the large quantity of homogeneous substance which undergoes fibrillation in the peritoneum, with coincident elongation of the cells, it is difficult to make any positive statement. It can only be said, with certainty, that the fibrils originate at the expense of a large continuous mass by a kind of transmutation.*

Further investigation has shown the original interpretation of Schwann to be the correct one, and that the fibrillæ of connective tissue take their origin from elongated cells, either by the splitting up of the cell body into fine fibrillæ, or by the body of the cell becoming drawn out into one long fibrilla.†

The most probable view then is, that the homogeneous intermediate substance which appears at a certain stage of development in the peritoneal lamina originates in a continuous metamorphosis, extending irregularly towards the central portion of the rapidly enlarging cell substance of the formative cells. The lamina thus originating in the fusion of the metamorphosed cell substance becomes secondarily perforated with smooth-edged foramina, whilst a continuous conversion into fibrils takes place.

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* I extract from a letter of Babuchin to Stricker that Babuchin has convinced himself of the development of cells into fibrils in the gelatinous tissue of Fishes. He admits, however, that what he terms Fibrils, under certain circumstances contracted themselves towards the nucleus of the cells which became round, and then commenced anew to send forth processes. This latter statement furnishes me with the strongest evidence that Babuchin in his preparations has not had to deal with the fibrils of connective tissue.

† Breslauer, Max Schultze's *Archiv*, Band v., 1869.

As regards the growth of connective and tendinous tissue, the breadth of the fibrils in the fœtus amounts, according to Harting,* to 0·0010—0·0014 millimeters, and in the adult to 0·0007—0·0017 millimeters. As the fibres, therefore, do not increase in thickness, their numbers must augment. The amorphous connective tissue between the fasciculi of the tendons becomes larger in quantity. The tendinous fasciculi increase, not only in number, but in thickness. In reference to the latter fact, Obersteiner † has shown that the points from which the new formation proceeds are partly situated between the old fasciculi and the investing connective tissue, and partly in the investing connective tissue itself.

Observations have been made by Sertoli,‡ showing that the development of the reticulum and of the adenoid substance of the lymphatic glands proceeds from embryonic connective tissue, composed of a mass of uniform cells.

As regards the Ligamentum pectinatum iridis, the trabecular tissue in embryoes of five months old may be distinctly seen to consist of branched flattened cells, the substance of which is homogeneous and condensed, whilst in these trabeculæ remains are still visible of nuclei that at a later period become atrophied.

In regard to the genesis of the elastic fibres, very various views have at different times been expressed. Their origin from nuclei, which Henle long ago believed he had perceived, has been by Henle§ himself rendered doubtful. It has also been proved that they do not develop from cells in the mode described by Donders.|| The opinion is now generally held that there is an actual deposit in the form of fibres.¶

It is remarkable that the fibres, after their deposition, increase in thickness.

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* *Recherches Micrométriques sur le developpement des Tissus*, etc., 1845, p. 53.

† *Loc. cit.*

‡ *Wiener Akademie, Sitzungsberichte*, Band liv., p. 149.

§ Canstatt's *Jahresbericht für* 1851, p. 22, Band i.

|| *Zeitschrift für wissenschaftliche Zoologie*, Band iii.

¶ Henle, *loc cit.* Reichert, Müller's *Archiv*, 1852, p. 94. H. Müller, *Würzburger Verhandlungen*, Band x., p. 132; *Bau der Molen*, 1847, p. lxii.

Fat Cells in Connective Tissue.—In various parts of the animal body the connective tissue contains great numbers of cells, which, enlarging equally in all their dimensions, attain a considerable size, and have in their interior a large fat drop, completely filling them. The diameter of these cells reaches, in man, 0·2 millimeters. Their form is round or somewhat oval. Where such fat cells are deposited in great number in the connective tissue, they are divided into separate groups, or lobules, by strong trabeculæ. Each of these lobules possesses its own system of vessels, which, with their branches, reach into the interior from the surface, and are accompanied with fine bundles of connective tissue; here they divide into such numerous capillaries, that the smaller groups of cells or even the individual fat cells, are surrounded by vascular loops.

Certain regions of the body in man are especially characterised by the presence of such adipose tissue. Thus it occurs in the subcutaneous connective tissue, or panniculus adiposus, which is very abundant in various parts of the body, as in the mammary gland of the female, the pubic region, buttocks, and sole of the foot; in other parts it is less developed, but is only absent in some few places, as the eyelids and male sexual organs. Adipose tissue, moreover, is found in the omentum, mesentery, beneath the pericardium of the heart, and on the great vessels, around the kidneys, in the orbit, and in the fat humps and adipose masses formed in the bodies of certain animals, etc.

In the fattening of animals, or in commencing obesity in man, the adipose tissue increases at these points, and occurs in large quantities also in regions of the body that with less abundant supplies of food remain free from fat; as, for example in the connective tissue between the muscles.

In large and fully developed fat cells, a thin smooth membrane can be distinguished surrounding the oil drop, which, however, collapses and becomes folded, if the cells are burst by pressure, and the contained drop of oil be allowed to escape. The membrane of the fat cells can also be brought into view in a crumpled state by boiling the tissue with strong alcohol and ether.

The oil drop contained in these cells presents a faint yellow

tint in man, but in various animals many other tints occur. In the fresh cells, both of cold and warm-blooded animals, the fat is fluid. On cooling, it solidifies with great facility, especially in the latter class of animals. This last process occasions a flattening of the closely compressed cells, and their oily contents may frequently be observed to crystallize partially in needles which are collected in the form of a brush. When this occurs, a single spicule or a crystalline stella, composed of many spicules, appears on the surface of the fat cells.*

Besides the large fat cells enclosed in a smooth membrane, which are most abundant in fully developed adipose tissue, other cells also occur which are smaller, and in which the oil drops are invested by a layer of granular cell substance; this, when seen in profile, appears in the form of a rather broad ring around the oil drop. Cells presenting this aspect are frequently found at the borders of fat lobules, as in newly formed adipose tissue, whether in the embryo or in the adult. The formation of adipose tissue may be excellently followed in the omentum of animals as well as in certain cases of sudden death in man. In the first stage of their development, the cells that subsequently form fat cells appear as small round granular bodies, provided with round nuclei, and presenting all the characters of young cells. In the interior of these a few small strongly refractive oil drops first originate, which, however, usually soon collect to form a single large fat drop, occupying the middle of the cell. Much less frequently several large drops are found close to one another.

The protoplasm of the cells in which such large drops have developed, lies like a cincture around the drops, presenting everywhere nearly the same breadth, except only where the nucleus is imbedded in it and forms a thickening or projection that causes the whole protoplasmic mass to be comparable to a signet ring.

During the succeeding stages of development the cells undergo continuous increase in size, the oil drops in particular becoming larger. The investing protoplasmic layer, whilst it progressively diminishes, though not proportionately

* Henle, *Allgemeine Anatomie*, p. 393.

to the enlargement of the fat drops, preserves its original granular appearance. The nucleus is always visible, but, concomitantly with the increase of the oil drop, and the expansion of the surface of the protoplasmic layer, is constantly pressed outwards. In the final stages of development the remains of the original investment of protoplasm consist only of a thin homogeneous membrane, on some part of which the nucleus, now become somewhat more homogeneous and diminished in size, may always be demonstrated. The nucleus is best seen in cells treated with Müller's fluid, and then stained with carmine.

If we institute a comparison between the fat cells in various stages of their development, it becomes immediately apparent that the protoplasm originally present does not merely expand coincidently with the enlargement of the cells, but that as the cell attains its full growth, and becomes invested with the above-mentioned membrane, the protoplasm also augments in quantity.

We possess no information from direct observation, of the relation in which the protoplasm of the cell and the contained oil stand to one another in regard to their nutrition.

It is, however, certain, that wherever a new formation of adipose tissue occurs, a supply of histogenetic substance in the form of young cells first occurs, which is followed by a supply of material for the growth of these cells.

In consequence of hunger and disease, the fat cells lose their oil, and become filled with a serous fluid. In rabbits, Czajewicz* has observed the fat to disappear during abstinence from food in the course of a few days, and with equal rapidity, when abundant nutriment was supplied, reappear in the original cells.

Cartilage.

Of this tissue those organs of the animal body are formed either wholly or partially, which have long been noted in anatomy on account of the persistence of their morphological characters and great pliability, or from their peculiar consistence when cut. In histology, the distinction formerly made

* Reichert and Du Bois' *Archiv*, 1866, p. 289.

into proper (true, hyaline) cartilage, and fibrous cartilage is no longer admissible, since it has been shown that just as the former consists of cells imbedded in a transparent and apparently uniform matrix, the latter is composed of similar cells in a matrix traversed by fibres.

TRUE OR HYALINE CARTILAGE contains cells provided with nuclei (cartilage corpuscles) lying in cavities of various size and form distributed through an amorphous matrix, and the corpuscles closely resemble the cavities in their form.

In order to demonstrate these points, it is only requisite to make very fine sections of fresh cartilage. If it be desired to investigate cartilage in a physiologically fresh condition, only indifferent fluids can be employed, as in the case of connective tissue. For such observations those cartilaginous plates of cold-blooded animals which can be easily isolated from the soft parts, and are as thin as ordinary sections—as, for example, the ensiform process or the episternal cartilage of the frog, or the thin cartilaginous plates of the shoulder girdle of tritons—are preferable.

In such cartilages, the cells lying in the interior of the cavities appear when fresh as transparent, finely granular masses completely filling them up, and resembling the protoplasm of other cells. A small number of large granules are found in their interior, together with a well-defined round nucleus, containing several strongly refractile, large, and bright molecules, which are usually larger than those found in the protoplasm of ordinary cells, causing the nucleus, when compared with these, to present a coarsely granular appearance (fig. 6); the nucleus occasionally appears transparent and vesicular, with double contour lines and a single nucleolus. Two nuclei may frequently be seen in one cell. If, as in the case of connective tissue, an indifferent fluid be applied, like the aqueous humour, or serum diluted with distilled water, a cloudiness first occurs in the granular cell substance; the fine molecules originally present become partially concealed in portions of the cell substance which have rolled themselves into ball-like masses, and soon a shrivelling of the cell becomes apparent, so that it either partially or entirely separates from the wall of the cavity in

the cartilage; as a consequence of this a transparent ring appears between the inner surface of the cavity and the shrivelled cell, or the cell may still remain attached to certain points of the wall of the cavity, and is then irregularly stellate; such long and more firmly adhering processes of the already partially shrivelled cell usually detach themselves sooner or later, but do not shrink in the same proportion, so that even when completely detached from the walls of the cavity such cells appear to be irregularly beset with processes. If these appearances, which

Fig. 6.

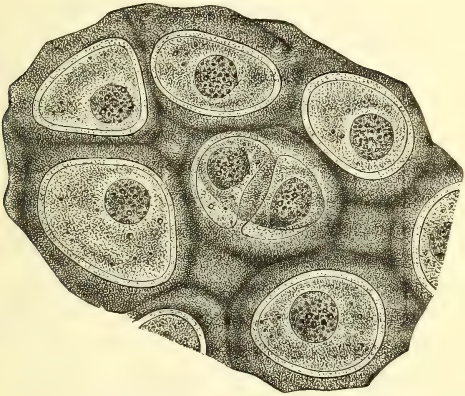

Fig. 6. Fresh cartilage from the Triton.

long remain unaltered, have been produced by the action of water, it may be seen that in some cells the nucleus has become indistinct, its place being indicated only by a dull spot; whilst in others it still appears distinctly defined. By changing the focus some of the indistinct nuclei may be more clearly brought into view, but others always remain indistinct; and these differences appear to depend upon the varying position of the nucleus in the cell, in consequence of which the greater part of the latter is sometimes above and sometimes below the nucleus in relation to the observer. Similar changes to those induced by the addition of water occur in the cartilage cell on the addition of saccharine and

saline solutions. Dilute solutions of potash and soda, and also of acetic acid, produce very similar effects.

The experiments of Heidenhain* have shown that powerful induction shocks cause contraction of the cartilage cells, render them irregular in shape, and detach them altogether or in part from the wall of the cavity. This was first observed by Heidenhain in the cells of the cartilage of the head of tadpoles, and in the articular cartilages of the adult frog. In the former he also saw the molecular movement of granules previously visible in the cells effectually stopped. In shrivelled cells there further occurred an accumulation of clear drops, or similar drops were thrust out into the cavities of the cartilage. The first action of the induction current is to produce a cloudiness in the interior of the cells, which often suddenly traverses them like a shadow. Heidenhain regards these phenomena as the expression of commencing coagulation, as are also all the changes induced by induction shocks, since he was unable to observe that the death of the cells was accompanied by any return to their original condition.

If one of the above-described induction apparatuses be used in order to apply a few opening shocks to the ensiform cartilage of the Frog (Rana temporaria) covered with a covering glass, and placed without addition of fluid upon tin-foil electrodes closely connected with one another, it will be found that an entire series of such shocks are always required to produce a distinctly visible change in the cells, or a long period after the application of a shock must elapse in order to allow the very slowly following change to become apparent. The cells of the cartilage of Tritons behave themselves very differently in this experiment. Here a single shock is sufficient to cause the cells to contract rapidly, and even quite suddenly, under the eyes of the observer, like transversely striated muscle when irritated; indeed, even the iron core may be removed from the primary coil, and the secondary coil of the apparatus previously quite thrust home may be withdrawn to considerable extent, and yet the strength of current will still be sufficient to produce the

* *Studien des Physiologischen Instituts zu Breslau*, Heft 2. Leipzig, 1863, p. 1.

same results with a single shock. The cells which have thus been made suddenly to undergo contraction (fig. 7) appear coarsely granulated, darker than before, with the nucleus scarcely, if at all, perceptible; whilst alteration of the focus, and close inspection of the edges of the cells after they have been separated from the cavity, shows that the immediate cause of their altered appearance is that their surfaces have become mulberry-like (fig. 7). In this condition the cells may

Fig. 7.

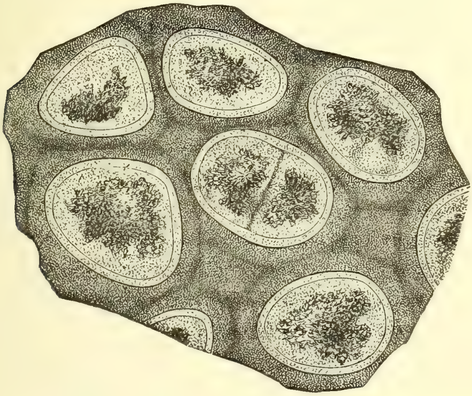

Fig. 7. Cartilage from a Triton after a single opening shock of induced electricity.

remain and be examined for hours, or even for days together, if they are preserved from the effects of evaporation by the employment of the moist chamber. A slight enlargement, accompanied by increased smoothness of the surface, may frequently be observed; the nucleus at the same time becoming somewhat more distinct; but the cells always remain more opaque than before the passage of the current, and never completely recover their original appearance. Nor are any satisfactory results obtained if the attempt be made to restore the cartilage to its normal condition by introducing it again beneath the skin of the animal. The cells do not recover their previous appearance even four and twenty hours or more after the application of the electrical shock. For the second observation

some portions of the cartilage should be preserved which were not situated between the electrodes in the first experiment for the sake of comparison. It must be admitted that a vital contraction of the cartilage cells has not been clearly proved to occur so long as it has not been shown that they are not liable to alterations of quiescence and activity, or, in other words, do not undergo amœboid changes of form. The effect which a single induction shock produces in the cartilage cells of Tritons renders it, however, highly probably that their diminution is due to a contractile power. On a warmed stage an alteration in the cartilage cells of Frogs and Tritons is first observed when the temperature rises to 73° or 75° C. (163°—167° Fahr.); the cells then become cloudy, in consequence of the formation of a granular coagulum. Nothing further has been remarked respecting the differences in the peculiarities of the cells of hyaline cartilage in various animals besides that which we have above stated in regard to the cells of the Frog and Triton. The observations made by Reitz* on the cells of the tracheal cartilages excised from Rabbits, in reference to the formation of cicatrices, and their behaviour in inflammation of the trachea produced by caustic ammonia, are well worthy of notice. In these experiments the cartilage cells in the cicatricial tissue were seen to assume the form of elongated fibres, and those of the irritated cartilage to become mulberry-like, with numerous deep depressions, as though about to divide. That wounds of cartilage heal by connective tissue is an old observation.†

As a general rule the appearance of the cells of hyaline cartilage agree more closely with the formerly described characters of fresh cartilage from the Amphibia, the more recent they are when brought under examination.

In cartilages longer removed from the body the cell substance appears cloudy and shrivelled, and more or less completely

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* *Sitzungsberichte der Wiener Akademie*, Band lv., p. 501.

† See G. H. Weber on this subject in Hildebrandt's *Anatomie*, Band i., p. 305. More recently, Redfern has published his observations on the same subject. See Henle, *Jahresbericht für* 1851, p. 52; also Klopsch, *Zeitschrift für klinische Medicin*, 1855.

detached from the wall of the cavity; the nucleus varies in distinctness, and is sometimes homogeneous and sometimes granular. Cells are frequently observed in the costal or laryngeal cartilages, containing deep yellow-coloured drops (of oil), surrounded by dark rings, more or less strongly refracting light. Similar drops are often found free in the cavity of the cartilage, external to the shrivelled remains of the cell.

The cells, and the cavities of the cartilage in which they are lodged, are separated by a variable amount of the matrix; they, moreover, sometimes lie detached and separate at regular distances, whilst at others they are united together into groups of few or many cells; and these again may be separated from one another by wide intervening spaces or by a few solitary cells. Two or more cells lying in close proximity to one another are frequently seen to occupy the same cavity. The form of the cartilage cavities is spheroidal, ellipsoidal, or elongated and fusiform, or somewhat flattened and lenticular; the two latter forms occurring closely compressed together, near the free surfaces that play over one another in joints, or in many of those cartilages whose surfaces are invested by perichondrium, and the cells then lie with their long diameter parallel to the surface; whilst in the more centrally situated portions of these cartilages are the larger cavities of the first-named varieties, and between these and the most external, various transitional forms. At points where cartilage and bone tissue are in immediate apposition the cartilage cells are frequently found to be arranged with great regularity in longitudinal rows in the direction from the bones towards the free surface of the extremity invested with cartilage. The cells in these longitudinal rows will be subsequently considered in treating of the subject of ossification. The cartilage cavities occasionally present a stellate form. Statements to this effect may be found in the writings of Leydig,* where he is describing the skull of the Chimæra and various Plagiostomatous fishes. Stellate cells have also been found by Kölliker† (in softer parts ?) in the tracheal cartilages of oxen.

The matrix of hyaline cartilage, when in a perfectly fresh con-

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* Müller's *Archiv*, 1851, p. 241.

† *Gewebelehre*, 1867, p. 69.

dition, and examined in thin sections or laminæ with very high powers, often presents a thoroughly homogeneous appearance. But it also happens that in recent and very transparent cartilages, especially in those in which the cells lie close together—as, for instance, in the earlier-mentioned examples of cartilage from the Frog and Triton—the cells are apparently surrounded by clear rings of equal breadth; and that the small trabeculæ extending between the adjoining cells only represent the circular layers investing these cells. In the older cartilages of various animals and of man there may also frequently, but not always, be seen a similar circular area which sometimes appears as though composed of several concentric rings. According to Max Schultze, this appearance is very beautifully exhibited in the cartilage of the Myxine. These rings represent the transverse section of the successive shells deposited around the cartilage cells, constituting the so-called membrane of the cartilage cell, or cartilage capsules of authors. We shall learn their significance hereafter. By the application of certain reagents, as, for instance, diluted sulphuric acid and chromic acid,* or a mixture of water, nitric acid, and chlorate of potash, or by digestion in water, at a temperature of from 35° to 40° C.† (95° to 104° F.) (in which case the addition of acids, in order to convert the connective tissue as usual at a lower temperature into gelatine, operates very effectually) the matrix of the cartilage, however homogeneous it may appear to be in the fresh condition, may be split up so completely into a number of layers arranged concentrically around the cells, that nothing remains besides them; and, indeed, in more fully developed cartilages a series of precisely similar shells succeed that which immediately surrounds the cell; or there may appear two or more closely approximated cells, with their primary capsules enclosed in secondary capsules, and groups of the latter again enclosed in still larger ones. It is only in cartilages with sparingly distributed cells that a portion of the firm matrix at a great distance from the cells surrounded with

* Fürstenburg, Müller's *Archiv*, 1857, p. 1.

† Heidenhain, *loc. cit.*, pp. 23 and 25.

concentric areas, remains unlaminated after the operation of the above-mentioned agents.

The imbibition of the red colouring matter of anilin is well adapted to exhibit the layers of the capsule.* The lamination of the tissue is also excellently shown by the action of chloride of gold, and very beautiful preparations can be obtained by protracted treatment with this agent, in consequence of the deep colour communicated by the reduction of the metal.

If diluted sulphuric acid or concentrated hydrochloric acid acts for a long time upon these sections of cartilage, the largest capsules first dissolve, and then the secondary ones. Those which immediately surround the cells are the most resistant. Moreover, if sections of cartilage are long boiled, we may first remark the above-described lamination of the matrix, and then successive solution of the capsules in the order above given. All these operations consequently lead to the isolation of the cells still invested by their capsules, providing they are subjected to their influence only for a certain definite period. The observations above adduced completely negative the views of those who regard the clear rings around the cartilage cavities as a mere optical phenomenon, and who deny the existence of the cartilage capsule.†

The ultimate result of continued boiling is, however, that the coagulated cells alone remain.‡ The solution obtained from cartilage after exposure to a boiling temperature for twenty-four hours, or for a few hours only at a temperature of 120° C. (248° F.), gelatinizes on cooling like gelatine itself. It does not, however, contain gelatine, but the material distinguished from gelatine by Johann Müller, by the name of Chondrin. The opposite statement of Friedleben§ has been disproved by Wilkens‖

* Landois, *Zeitschrift für wissenschaftliche Zoologie*, Band xvi., p. 11.

† Bergmann *Disquisitiones Microscopicae de Cartilagine. Mitau und Dorpat*, 1848.

‡ Hoppe, *Archiv für Pathologischen Anatomie*, Band v., p. 174. See also Mulder and Donders in G. J. Mulder's "Essay on General Physiological Chemistry;" Donders, in *Höllandische Beiträge, Düsseldorf. u. Utrecht*, 1846; Zellinsky, *De telis quibusdam collam edentibus, Diss. inaug.* Dorpat, 1852.

§ *Zeitschrift für wissenschaftliche Zoologie*, Band x., p. 20.

‖ *Idem*, p. 467.

and Trommer.* The chondrin-giving substance of cartilage, unlike the gelatine-yielding substance of connective tissue, does not swell up in water. Acetic acid causes it, when obtained from some cartilages, to become somewhat clearer, whilst in others it renders it cloudy. It does not cause it to swell up.

After exposure for from eight to twelve hours to the action of solution of osmic acid, containing one-fortieth per cent., thin sections of cartilage exhibit a system of dark striæ, usually running in a straight direction through the matrix, which frequently connect the several cell cavities with one another. Bubnoff,† in describing these striæ for the first time, expresses his opinion that they are to be regarded as juice canals.

The divisibility of the matrix of hyaline cartilage into capsules of various orders, or cell territories as they have been termed, shows that we cannot regard the matrix as an excretion of an amorphous and uniformly dense intercellular substance between the cells, as was formerly held to be the case before the exact value of the facts above stated was recognised; though this is a view to which we shall again refer in our account of the development of hyaline cartilage. It has not yet been shown whether, in hyaline cartilage, an intervening material different from the chondrin-yielding substance, and which, if present, would be in smaller quantity than the former, really exists or not.

The various parts of the embryonic skeleton are formed from hyaline cartilage, whilst in adults it constitutes the cartilages covering the articular ends of bone, and the opposed surfaces of the symphyses, the ensiform process, the ribs, and lastly, the bronchial, tracheal, and laryngeal cartilages, with the exception of the epiglottis. In the lower Vertebrata, Fishes, and Amphibia, considerable portions of the skeleton, which are ossified in other animals, remain cartilaginous throughout life; whilst in some animals cartilages occur in parts which, in others, and in man, consist only of connective tissue; as, for instance, the sclerotic coat in the eye of Birds, Amphibia, and Fishes. In regard to the Invertebrata, descriptions have been given of

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* Virchow's *Archiv*, Band xix., p. 554.

† *Wiener Sitzungsberichte*, 1868, April.

the distribution and occurrence of cartilaginous tissue, in the case of Cephalopods and Molluscs, by Lebert and Robin,* and by Claparède and Semper.† Before we pass to the consideration of fibro-cartilage, the fibrous transformation of the matrix of hyaline cartilage must first be mentioned, which occurs sooner or later after the commencement of extra-uterine life. This appearance is particularly obvious in the costal and laryngeal cartilages.‡ On examining a transverse section of the costal cartilages of an adult, striæ or rings may almost always be observed, distinguished by their white and opaque appearance, and the peculiar lustre they possess. Microscopic examination shows that the matrix at these points is composed of rigid closely approximated parallel fibres. These are unbranched, and when subjected to the action of acetic acid, do not disappear, but pass uninterruptedly into the surrounding non-fibrous portion of the matrix. If such a section be broken up with needles, the parallel fibres break at various points of their course, and these project to a variable extent from the fractured surface; the cause of this development of fibres in hyaline cartilage is not accurately known. Coincidently with the formation of these fibres in cartilage, a process of proliferation usually occurs, so that the cells lie closely compressed in great masses in the matrix.§

FIBRO-CARTILAGE.—True fibro-cartilage differs from hyaline cartilage in its matrix, presenting fibres of variable number, form, and chemical characters. The alteration of the index of refraction occasioned by the layers of delicate fibres and their interstices, and in some fibro-cartilages the small degree of translucency possessed by the several fibres, makes even fine sections of these cartilages, when compared with hyaline cartilage, appear on examination much darker and more opaque. By direct light, on the other hand, the fibro-cartilage

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* Müller's *Archiv*, 1846, p. 129.

† *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 274.

‡ Donders, *Holländische Beiträge*, Band i., p. 258. H. Meyer, Müller's *Archiv*, 1846, p. 292.

§ Donders, Meyer, *loc. cit.*

appears whiter or more yellow in comparison with the hyaline variety. It is less brittle, but often cleavable in certain directions. The latter circumstance enables a mechanical isolation of the cells, on breaking up such sections of cartilage, to be much more easily accomplished than in hyaline cartilage.

The fibres of *elastic or reticular cartilage* (fig. 8) appear dark, of unequal thickness, branched, and often intercommunicate by very numerous anastomoses, thus forming a very fine but often wide-meshed plexus. In their general characters and capabi-

Fig. 8.

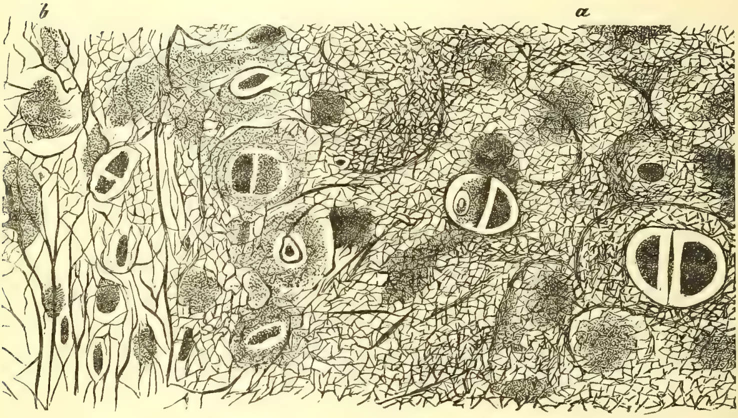

Fig. 8. Section of the boiled and dried auricle of the ear of Man; *a*, retiform cartilage; *b*, connective tissue.

lity of resisting the action of acetic acid and alkalies, they agree with elastic fibres. In many instances, as in the cartilage of the ear of man, and the epiglottis, it may be shown that these fibres are uninterruptedly continuous with the elastic plexus of the connective tissue investing the cartilage (Donders). The close fibrous plexus often reaches to the margin of the cavities, which contain the cells of the cartilage, but frequently a homogeneous capsule remains around the cartilage in the form of a clear ring, whilst a considerable quantity of the matrix between the fibres may remain distinguishable, and both conditions occur in close proximity with one another in the same cartilage. As various

cartilages present differences in respect to this point, so do we find some giving more some less chondrin on boiling. The fibrous material does not itself undergo solution on boiling. A beautiful object for the observation of the above-mentioned transition of the elastic fibres of cartilage into those of the skin, is afforded by sections made through the auricle of man, first boiled for a short time as a whole, and then dried (see fig. 8).

Moreover the fibres of the fibro-cartilaginous extremity of the processus vocales of the arytenoid cartilages pass immediately into the elastic fibres of the vocal cords.* This latter fact is opposed to the view maintained by Gerlach,† of the specific distinctness of the fibres of plexiform cartilage. The parts composed of elastic fibrous—or retiform—cartilage consist in man of the auricle of the ear, of the epiglottis, and the extremity of the processus vocales of the arytenoid cartilages (Rheiner).

CARTILAGE MINGLED WITH CONNECTIVE TISSUE.—Cartilaginous tissue occurs, and frequently in very considerable masses, imbedded in connective tissue. Efforts have in consequence been made to establish a special group of fibro-cartilages, the connective-tissue cartilages; but it would appear to be more correct to describe these structures as mixtures of the two tissues. Such mixtures occur in the interarticular cartilages, the glenoid cartilages, the cartilages of the symphyses, at the articular extremities of the clavicle, and the corresponding articular surfaces of the scapula and sternum (Henle), and in the tarsal cartilages of the eyelids. With these must also be enumerated the tendons and tendinous sheaths containing cartilage. Such tendon-cartilage may be frequently observed in the tendons near their attachments to bone. The Tendo Achillis of the Frog must especially be mentioned as presenting large cells with round nuclei, which may be regarded as cartilage cells, and which are present in considerable numbers.‡

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* Rheiner, *Beiträge zur Histologie des Kehlkopfes.* Würzburg, 1852.

† *Gewebelehre*, p. 124.

‡ Kölliker, Lehmann, *Zeitschrift für wissenschaftliche Zoologie*, Band xiv., p. 109, Taf. 14.

Also the appearance which has already been described in the digital tendons of the Frog may again be alluded to. The same features are presented by other tendons, especially amongst the Amphibia. It must, however, here be stated that objections have been raised to considering these cells to be cartilage cells.* It is certain that in the cells of these tendons of the Frog no chondrin-yielding substance can be proved to be present. In preparations treated with chloride of gold, masses of equably stained protoplasm are found in close apposition.

Parenchymatous Cartilage (Cellular cartilage).—We must now describe a form of cartilage which possesses no matrix, the so-called parenchymatous cartilage. Kölliker† has also sought to introduce this type amongst the tissues. Thus, amongst the cartilages without intermediate substance, he enumerates the chorda dorsalis of embryoes and of many adult fishes, numerous fœtal cartilages, some parts of the cartilage of Myxinoid fishes, a part of the branchial laminæ of fishes, the cartilage of the Tendo Achillis of the Frog, and of the outer ear of many Mammals; the cartilage entering into the structure of the Geryonia, Annelida, Cephalophora, and of Limulus. This grouping, however, is decidedly imperfect. Kölliker distinguishes between the capsule or membrane of the cartilage cells, consisting of chondrin-yielding substance, and an intercellular substance existing between the cells, but also yielding chondrin on boiling; but, inasmuch as all the chondrin-yielding substance of cartilage is referrible to the capsules, a number of the cartilages described by Kölliker as destitute of intermediate substance must be regarded as belonging to the hyaline cartilages. How far, on the other hand, we are justified in speaking of naked cartilage cells, and of considering the cellular form of cartilage as composed of them, is not as yet determined.

On this point we can only refer to embryological observations,

* Gegenbauer, *Jenaische Zeitschrift für Medicin und Naturwissenschaften*, 1866, p. 307.

† *Gewebelehre.* Leipzig, 1867, pp. 66, 67.

and to others based on comparative anatomy, and thus allude, for instance, to the early stages of cartilage, to the primordial cells of cartilage and the tissues composed of them.

In order, however, to diagnose the cells as cartilage cells, of whose history and development we have no information, it is requisite that we should be better acquainted with their internal organization than at present, as well as with the differences that exist between cartilage cells and other masses of protoplasm. Other difficulties similar to those that are here met with in regard to the limitation of the cartilaginous tissue, frequently arise when the identification of cells is under consideration. Experiments undertaken to determine whether in the cells contained in the Tendo Achillis, and in the digital tendons of the Frog or Triton, similar phenomena follow the application of induction shocks to those observed in the cells of the hyaline cartilages of these animals, have altogether failed.

Development of Cartilage.—Hyaline cartilage exhibits in most instances an unmistakable similarity to the first rudiments of all animal tissues, in being composed of cells advanced to a nearly equal grade of development.

The investigations of Rathke* on chickens, and of Kölliker† on tadpoles, have taught us that the embryonic cells whilst still filled with yolk granules, as they gradually increase, become more transparent; and then becoming separated from each other in consequence of the development of rods of a homogeneous and transparent substance, finally constitute the first rudiments of embryonic cartilage.

As soon as the matrix has become distinctly differentiated from the previously closely compressed cells, it forms a homogeneous clear ring around each, and between these rings run fine lines resembling the contour lines of epithelial cells. At this period, therefore, the cartilage consists of cells which are contained in polyhedric capsules, and no special artifice is required in order to isolate the cells completely, together with their capsules. The costal cartilages of young sheep, or of human

* Froriep and Schleiden's *Notizen*, Band ii., 1847, p. 305.

† *Mikroskopische Anatomie*, Band ii., p. 349.

embryoes kept in Müller's solution, can easily at this stage be split with needles into laminæ.

In pursuing the further development of cartilage, the question arises of the capacity of cartilage cells to undergo division. Cells in the act of division, or apparently originating from the division of cells, are frequently met with, not only in embryonic cartilages, but also in those of adults. Thus, in the first place, cells may be observed containing two nuclei. It has also been stated that the nucleoli are sometimes double, nor is it difficult to demonstrate this in the cartilages of tadpoles. The division of the nucleus has even been directly observed (as recently by Kölliker).* The occurrence of two nuclei appears, however, to be the only condition which is of frequent occurrence and easily observed.† It is not easy to decide whether in these cases two new nuclei have originated in the place of one nucleus that has undergone absorption, or whether the division of the nucleus on account of its rapidity has escaped observation. The division of the cell itself may, indeed, be readily followed, since it depends on the formation of a groove encircling the cell. It cannot, however, be stated that the division leads in the first place to the formation of two nucleated protoplasmic masses, lying in a common capsule. It would rather appear that the division of the protoplasm is very intimately associated with the formation of a capsular investing sheath for the daughter cell. However closely the cells under observation lie in apposition to one another, it is still observable when they are detached from the walls of the cavity by some of the above-mentioned means that the cavity is itself divided by a thin septum into two chambers. The differentiation of parts in the entire plane of division consequently takes place with great rapidity. The daughter cells are capable of forming complete capsules, which gradually increase in thickness, and are clearly to be distinguished from one another, not only where they are in contact, but also where they touch the capsule of the mother cell.

The daughter cells originating in division can in like manner

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* *Gewebelehre*, 1867, p. 24.

† Frey, *Histologie and Histochemie*. Heidenhain, *loc. cit.*

produce a new generation, leading to enlargement of the spaces enclosed by the capsules of the mother cells.

The cells then appear to be arranged in detached groups at a considerable distance from one another, and the youngest capsules are now more distinctly visible. After the application of the means which have been above described, the whole matrix again presents the appearance of being divisible into nests of capsules, one enveloping the other.

If we further compare the appearances presented by embryonic cartilage with the fully developed cartilage of adults, we must admit that the cells, without undergoing division, are capable of producing successive generations of capsules, fresh ones constantly forming in the interior of the old, whilst the external ones increase in size, and become faintly marked as regards their limits. In such cartilage the cells appear fewer in number, and the matrix of the cartilage just formed can be frequently artificially split into concentric rings surrounding the cells. In fully developed cartilage, moreover, both laminated mother and daughter cells may be coincidently observed.

Observation of the development of cartilage thus teaches us that in its earliest stages cells destitute of cell membrane or primordial cells are alone present, and that the so-called matrix or chondrin-yielding substance of cartilage is a secondary formation. Opinions are, however, divided respecting the relation which the latter bears to the former.

On the one hand the chondrin-yielding substance may be regarded as a purely intercellular material, which is either deposited between the cells from without, or is a secretion of the cells themselves. In order to explain the nature of the capsules (including the youngest) it must be admitted on this view that the intercellular substance in the vicinity of the cells is differentiated by a peculiar (?) process of condensation from the remaining intercellular substance.*

In complete opposition to this exposition of the nature of the matrix is the view propounded by Remak,† to the effect

* Aeby, *Zeitschrift für rationelle Medicin*, Band iv., 3 R., p. 43.

† Müller's *Archiv*, 1852, p. 69.

that the young cartilage cells are provided with two membranes, of which the innermost corresponds to the primordial utricle of the vegetable cell. In the act of cell division this last alone participates. The proper substance of the cartilage is deposited either between the external and internal membranes, or between the former and the daughter cells, and indeed, in the first instance, on the inner surface of the external membrane; and in this mode the vesicular cavities in the cartilage arise. Each newly developed daughter cell immediately forms again an external membrane, upon the inner surface of which fresh cartilage is deposited, whilst the cells again subdivide; and there is thus developed a nest of cartilage cells contained one within another. By the fusion of the several cartilaginous laminæ with one another, and the disappearance of the cell membranes which served as a framework for its deposit, the matrix of the cartilage is produced, which thus appears to be an intercellular formation, and may be called "parietal substance." It is easy to perceive that the views of Remak were constructed on the cell theory of his day.

If, however, we abstract the two hypothetically present membranes of Remak, the formation of chondrin-yielding substance, described by him, and its relation to the cells, corresponds exactly to the processes observed in the development of cartilage, and to the appearances which may be obtained by breaking up mature cartilage. Fürstenberg, who was the first to accomplish this, regarded the layers of chondrin-yielding substance as thickened cell membrane, and showed that in certain cartilages the whole matrix was to be considered as composed of such thickened membranes belonging to successive generations of mother and daughter cells. Kölliker* also maintains the capsules of cartilage to be cell membranes, and to represent the secondary membrane of the vegetable cell. In some few cartilages the matrix is composed of these alone, but in others again, especially in those in which the division into cell territories is not completely effected, a large and often the chief part of the matrix is formed of pure intercellular substance lying between the cell membranes. Kölliker's view is

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* *Gewebelehre*, 1867, p. 64.

unsatisfactory on account of its attributing a double and consequently fundamentally distinct mode of origin to one and the same substance—that, namely, which yields the chondrin; and it is unlikely, therefore, to be correct. If, however, we adopt the view of Fürstenberg, which may be directly proved in the case of many cartilages, it is easy to show that in those cases where the lamination of the matrix is not completely accomplished, a portion of the original cell boundaries vanishes after the action of reagents, just as in most cartilages before the action of reagents they are likewise indistinguishable. It still, however, remains a question whether we shall represent the generations of capsules, of which the matrix of cartilage is composed, as new formations proceeding from the surface of mother and daughter cells, or as metamorphosed superficial layers of the cell protoplasm. The latter view is held by Max Schultze, Brücke, and Heidenhain; the two latter investigators, however, remark upon the difficulty of disproving the opposite view, and Heidenhain refers to cases where minute cells are surrounded by strong laminated capsules. It remains to be investigated whether isolated cells can undergo complete chondrogenous metamorphosis, and whether it can thus be explained how it happens that the matrix is frequently to be observed destitute of cells for a considerable extent.

According to Harting's researches on the cartilages of the ribs, the cartilage cavities increase in size throughout the period of fœtal life, and also after birth. The number of cartilage cavities in the newly born child is three or four times greater than in the fœtus, whilst in adults it is scarcely half as great as in the new-born child. In adults the cells are arranged more in groups than in newly born children, and in these more than in the fœtus.

As regards the growth of permanent cartilage in length and thickness, but little is positively known. It is impossible to admit that isolated cell formation in the interior of a large cartilaginous mass can cause an increase in its volume.

The result would, however, be different if the process of division were frequently repeated at the surface, or between two definite cleavage planes throughout the entire mass of the

cartilage. Phenomena of growth of the latter kind are, as we shall hereafter see, to be very beautifully observed in ossifying cartilage. Whether a deposition of new cartilage on the old is effected by the perichondrium, as some authors suppose, is a matter still requiring further observation. Very recently attention has been drawn by Bubnoff to the fact that cartilage is traversed by vessels, the tunica adventitia of which sometimes undergoes conversion into cartilage. The relations of the walls of the canals traversing cartilage in which vessels run, to the process of growth, it is therefore obvious, also require investigation.

In their early stages of development, reticulated cartilages are hyaline, and they retain this condition up to the third or fourth month of fœtal life. Fibres make their appearance about the fifth month. Here, as in the elastic fibres of connective tissue, the formation of the fibres can only be traced back to a deposit of fine fibres in the matrix.*

Calcified Cartilage.—A deposit of the salts of lime frequently occurs in the matrix of hyaline cartilage.

We shall hereafter trace more carefully such calcification of true cartilage in the embryonic cartilaginous skeleton, as a preparatory stage of intracartilaginous ossification. Calcification of true cartilage also occurs, in which the calcified tissue persists throughout life. Such cartilage was first described with accuracy by J. Müller,† in the cortex of the skeleton of the plagiostome fishes, under the name of tesselated calcified cartilage.

Calcified cartilage occurs also, as was shown by H. Müller,‡ in a persistent condition at the limits of ossification of the embryonic skeletal cartilage, as, for instance, subjacent to the articular cartilages, at the junction of the ribs with the cartilages of the ribs, and at the synchondroses of the

* Rathke, *loc. cit.* Rabl-Rückhardt, Reichert and Du Bois' *Archiv*, 1863, p. 41.

† Poggendorf's *Annalen*, 1836, p. 347.

‡ *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 51.

vertebræ and pelvis. It is rare for true bones and uncalcified cartilage to enter into direct contact with one another.

Calcification also occurs in cartilages which, like those of the larynx, begin to ossify with advancing age. In such cartilages it often happens that, notwithstanding parts are found in which both to the eye and touch earthy matters appear to be deposited, examination with the microscope reveals the presence of no true bone, but only of calcified cartilage. Reticulated cartilage only calcifies exceptionally in certain animals, as in the dog.*

Osseous Tissue.

Osseous tissue forms in man the principal constituent of the bones of the skeleton, and of the cementum of the teeth. This is equally true of all Vertebrate animals. A number of osseous fishes, however, instead of having their skeleton composed of true bone, present a homogeneous or fibrous osteoid substance, traversed by dentine-like tubes which may become actual dentine.† Taking the vertebrate series as a whole, the osseous tissue is widely distributed, since certain parts which are elsewhere composed of soft tissues, as the skin, tendons, and sclerotic coat of the eye, in some animals contain bone. In man, also, osseous tissue occurs in some soft parts as a pathological formation.

Structure of Osseous Tissue.—In a histological point of view, we distinguish in the first place in osseous tissue the matrix and the bone corpuscles. The distinction between these two constituents of bone may be easily perceived on microscopic examination, by transmitted light, of the frequently well-developed thin osseous plates that occur in pathological ossifications, or of the laminæ of the vomer, lachrymal bones, etc., or of fine sections prepared from the larger bones. The corpuscles appear as dark black figures, which consist of a central area, which is

* H. Müller, *Würzburg naturwissenschaftliche Zeitschrift*, Band i., p. 92.

† Kölliker, *Ueber verschiedene Typen in der Mikroskopischen Structur des Skelettes der Knochenfische*, "On the various Types of Microscopic Structure in the Skeleton of Osseous Fishes." Aus dem ix. *Bande der Würzburger Verhandlungen.*

either of large size and elliptical, or smaller, and then resembles the section of a bi-convex lens, from which delicate, greatly attenuated, and branched fibres are given off (bone canaliculi). The canaliculi proceeding from different corpuscles intercommunicate,* and thus connect the dark areas with one another.

The dark markings are distributed through a clear matrix

Fig. 9.

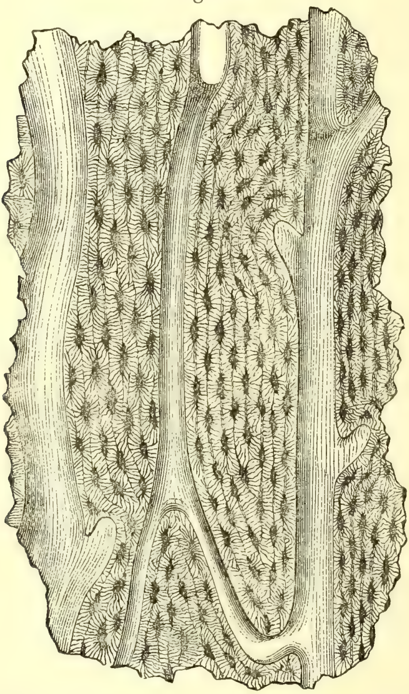

Fig. 9. Longitudinal section of human ulna.

(fig. 9); the material in which the corpuscles are situated either appears quite homogeneous in the form of a lamina, or is perforated by variously arranged spaces, which are often so large and numerous that only a network of bony trabeculæ of

* Kruckenberg, Müller's *Archiv*, 1849, p. 412.

various thickness is left surrounding them, or the spaces may be of relatively small size, in which case the surrounding substance is split by parallel, straight, or annular lines, into a series of ribbon-like laminæ, to which the corpuscles are attached with tolerable regularity in successive rows.

The dark markings caused by the corpuscles appear equally delicately white and lustrous, if the section is examined by direct instead of transmitted light.

The bone corpuscles and canaliculi were first described by Purkinje and Deutsch.* J. Müller† first pointed out the connection existing between the two, and at the same time expressed his opinion that the entire system of these corpuscles and canaliculi was filled with lime, on which account they were for some time described as corpuscula and canaliculi chalicophori.

The matrix of bone which, as follows from what has been stated above, frequently exhibits a well-marked lamellar structure, is brittle and friable, and confers upon it its peculiar consistence. If a portion of bone be treated with diluted acids, which expel the carbonic acid from its combination with lime, and render the latter as well as the phosphate of lime soluble, the bone becomes soft, whilst it preserves its original form. The softened remains of the matrix represent its organic basis, the so-called *bone cartilage* or *ossein;* and this, on being boiled with water, is converted into gelatine, though more slowly than collagen is obtained from connective tissue.‡

Bones thus softened in acids are well adapted for the preparation of fine sections for the microscope, and present the same appearances as those already described, except that the bone corpuscles now appear by transmitted light more transparent than the matrix.

If lime-containing bones are boiled for a long time, the organic material is in great part or completely removed, and the *earthy matters* of the bone remain behind, still preserving their original form. Chemical examination shows that these

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* *De Penitiori Ossium Structura,* 1834.

† Müller's *Archiv,* 1836, p. 6.

‡ Kühne, *Physiologische Chemie,* 1866, p. 391.

earthy matters consist in proportions varying with the animal, and the bone, of a mixture of carbonate of lime, of tribasic phosphate of lime and magnesia, of fluoride of lime, chloride of sodium, and traces of sulphates and of silica. The organic and mineral constituents of the matrix of bone, which are thus capable of being separated from one another, are so intimately blended together both in moist recent and in dried bones, that even with high microscopic powers no distinction can be perceived between them ; such, for instance, as a granular precipitate distributed through an organic basis.

It has not been accurately ascertained whether the osseous substance is composed of an intimate mechanical mixture of two molecules, or of a complex double molecule.* In various as yet imperfectly understood diseases (Rachitis, Osteomalacia), the bones lose their mineral matters, and, undergoing other concomitant changes, become soft, flexible, and capable of being cut, whilst the bones of old people, with coincident signs of atrophy (thinning, expansion of the cavities), become more rich in mineral substances, less elastic, and at the same time more brittle.

The coarse morphology of osseous substance, as seen under the microscope, consists then, as already mentioned, of plates, fibre-like trabeculæ, and superimposed lamellæ. The appearances presented in any particular case are dependent upon the osteological importance of the bone examined, upon the direction of the plane in which the section is made, and upon the part of this plane selected for examination.

Osteologists, as is well known, arrange the bones into different groups, as the long or tubular bones, flat bones, and short bones; and structural variations are met with corresponding to these divisions. In the short bones and in the apo-

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* According to the younger Milne Edwards (*Annal. des Sci. Nat.*, 4 S., Tom. xiii., p. 113), different bones yield tolerably constant proportions of ossein and bone earth. But the conclusions to be drawn from all previous analyses of bone are not in accordance with this statement. On feeding animals with unusual diet, as, for instance, withdrawal of flesh from the food of a carnivorous animal, even if the bones are coincidentally supplied with non-nitrogenous material, they become poorer in salts.

physes of the long bones, the osseous tissue forms a thin layer of compact substance on the surface; but in the interior small laminæ exist, inclined at various angles to one another, between which are medullary spaces containing vessels and connective tissue with marrow and fat cells. The substance of the bone consequently here presents a spongy character. In the flat bones, tables of compact substance, corresponding to the two principal surfaces, are superficially placed, between which the osseous substance presents the same spongy character. The compact bony substance is strongest in the diaphyses of the long bones; but even here, in the more internal parts which surround the great medullary cavity, it presents the spongy character which is more conspicuous in proportion as the epiphyses are approximated.

On making fine sections of the compact substance of the tubular bones after removal of the mineral matter, some of the finer characters may be very distinctly brought into view. Sections carried perpendicularly to the long axis of the bone exhibit larger or smaller round or slightly oval spaces, which are seldom elongated in a longitudinal direction, but are often bounded by slightly sinuous lines, and represent the transverse sections of the Haversian canals hereafter to be described. Around these the matrix of the bone forms concentrically arranged ribbon-like striæ, which, in a certain focus of the microscope, in the portion nearest to the canals, appear radially striated and somewhat darker than elsewhere. The number of laminæ succeeding one another from within outwards varies, but the smaller canals have fewer than the larger. As many as fifteen have been counted. The system of rings surrounding each space is enclosed by similar rings pursuing a course parallel to the external surface to the bone, so that the latter may be differentiated from the former as being of a higher order; but since the systems of the first order cease, in some instances nearer, and in others at a point more distant from the surface of the bone, the number of the rings running concentrically with the general circumference of the bone is not constant, but is smaller where the rings of the first order approximate more closely to the surface. Only those which course around the most superficial systems of the first order

completely surround the bone.* The spaces which remain between the systems concentric to the Haversian canals in the interior of the bone, and which present areas with three, four, or more angles, with incurved sides, are occupied by an interlamellar mass presenting a similar lamination. The interlamellar systems also, for the most part, run parallel to the surface of the bone; but it may also occur that they run parallel to the two opposite boundaries of the areas, and stand perpendicularly to others; or there may occur in the areas themselves, again, vertices of the systems of rings, which cut the direction of the closed systems at various angles, as shown in fig. 10.

But we frequently also meet with concentrically arranged systems of the first order, which have become flattened by

Fig. 10.

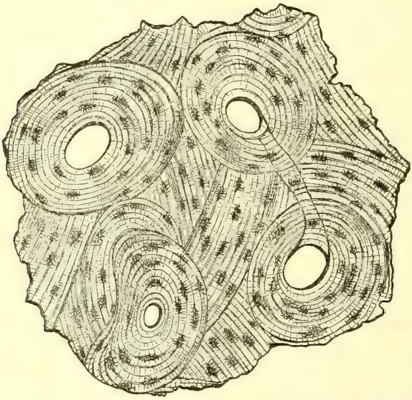

Fig. 10. Transverse section of human femur, deprived of mineral matter by hydrochloric acid.

mutual pressure, and are not separated by any interlamellar substance. The latter seldom occurs in the tubular bones of man, the former commonly occurs in animals.

Frey† calls the connective systems of the first order special

* Tomes and De Morgan, *Philosophical Transactions*, 1853, Vol. i., p. 109.
† *Histologie and Histochemie*, 1867, p. 280.

or Haversian lamellæ; the others, general or fundamental lamellæ. It is more important to distinguish the three series of Haversian lamellæ, intermediate lamellæ, and peripheric lamellæ.

The open or closed systems of rings seen in transverse sections of bone, are the transverse sections of lamellæ arranged around longitudinal and anastomosing canals, the transverse sections of which last constitute the spaces already described. Of this we may convince ourselves by making longitudinal sections of the long bones (fig. 9), in which the vessels may be seen to form elongated meshes. They either branch at acute angles, or if the branches are more divaricant, they soon follow a less divergent direction, or, which is more usual, they communicate by means of short oblique or rarely transverse branches, and pursue a course that is but slightly inclined to the long axis of the bone. The above-mentioned Haversian or medullary canals, opening upon the external surface of the compact substance, or into the medullary spaces of the spongy substance, are destined for the passage of blood-vessels. The spaces intervening between the Haversian canals are occupied by the ribbon-like longitudinal sections of the lamellæ. Portions of these lamellæ of the compact substance of the long bones may either be splintered off, or they may be obtained by sections made parallel to the surface. With high powers and a good microscope, a sharply defined punctation may be observed in them, besides also an indistinct, dull, veiny appearance, the whole substance being thus divided into a few bright islands.

The punctiform appearance is the expression of small round holes (sections of the bone canals to be hereafter described). The regular rhombs represented by Sharpey,* and observed also by Kölliker,† in his earlier preparations, appear to occur only under quite special conditions.

In complete analogy with the arrangement of the Haversian canals and lamellæ of the compact substance of the shaft of the long bones, is that seen in the compact substance of the

* An illustration of this, after a preparation of Sharpey, may be found in the large *Microscopic Anatomy* of Hassall, Taf. 30, fig 4.

† *Gewebelehre*, 1867, p. 186.

other classes of bones, when sections are carried through them in various directions, except that the relations are simplified in accordance with the smaller thickness here presented by the compact substance. The lamellæ again in these cases form the extreme boundaries of the bone; and if the thickness of the compact substance is very small, they may even constitute the entire mass of the bone.

The trabeculæ and lamellæ of the cancellous tissue present various forms, and in many instances the stronger trabeculæ are very regularly arranged, so that a kind of fibrillation is exhibited, which pursues a definite direction in regard to the surfaces of the bone examined. H. Meyer* has described such appearances in the bones of the lower extremity of man, and has shown that they stand in a certain relation to the importance of the bone as an organ of support. In the stronger trabeculæ and lamellæ of the cancellous tissue, Haversian canals may be seen with their concentric lamellar systems. In others we obtain, dependent on their more cylindrical or more flattened form, and the side from which they are examined, appearances similar to those offered by a flat view of the lamellæ of the compact substance; or else striæ and bands which form the limits of the trabeculæ in regard to the medullary spaces they surround.

We now turn to the consideration of the so-called *bone corpuscles* and their processes. The form of these in the bones of man is elongated and lenticular, and those of animals are for the most part very similar. When seen on the broad surface of the lamellæ, they appear elliptical; but seen on the small transverse section of the lamellæ, they resemble the transverse section of a bi-concave lens. In reference to their position to the lamellæ, they are found at the margins of the latter, arched in accordance with the curvature of the surface of the lamellæ where these form small arcs and adhering to their convex surface. In regard to their number, Welcker† counted in each square millimeter of the transverse

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* Reichert and Du Bois' *Archiv*, 1867, p. 615.

† *Zeitschrift für rationelle Medicin, N. F.*, Band viii., p. 232.

section of bone 740 on the average in man; the number varying from 780 to 800. Harting gives 910.

From these, as shown in fig. 11, the above-mentioned branched and anastomosing processes are given off in all directions, but especially at right angles to the lamellæ, and in the direction of the medullary canals. These processes do not, however, run in a single plane, but are much curved, and hence in thin sections of bone, whether transverse or longitudinal, we meet with them cut either transversely or more or less obliquely; and they may either appear still in connection with

Fig. 11.

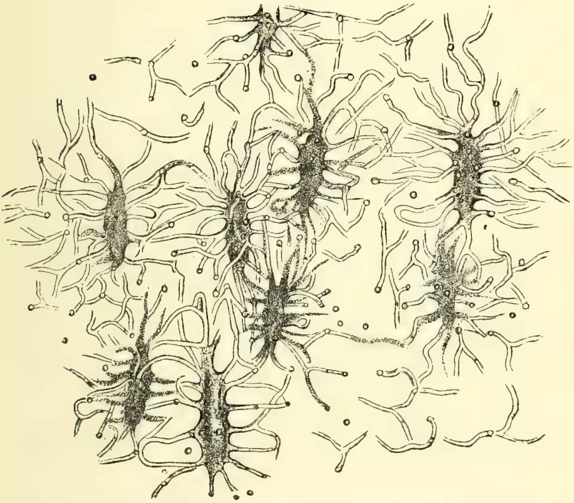

Fig. 11. Bone corpuscles with their processes, as seen in a thin section of human bone.

the corpuscles, or a portion only of their course may be seen; or, lastly, their communication with each other may alone be brought into view (fig. 11). In good sections the fine canaliculi may be followed either to the surface of the bone, or to the medullary canals and spaces where they terminate by open mouths, or they may reach to the ends of bones invested with cartilage, in which case they terminate in blind pointed extremities.

When the view already mentioned, which led to the terms corpuscles and chalicophorous canaliculi being employed to indicate the lacunæ and canaliculi, had fallen into disrepute because it had been shown by Lessing* that their dark appearance in dry bones on examination with transmitted light, and their white appearance with direct illumination, was to be ascribed to their containing air, and observers were therefore inclined to regard them as constituting a lacunar system, which in the living bones was filled with fluid; the researches of Virchow† again brought into prominence the view that these structures were corpuscles capable of being isolated. Virchow effected the isolation of the bone corpuscles by macerating the lamellæ in hydrochloric acid; but the same result can, according to Förster,‡ be obtained by means of nitric acid. A still better mode of procedure is to boil the bones deprived of lime with hydrochloric acid under pressure. In this mode F. Hoppe§ isolated very beautifully the bone corpuscles from the cutaneous plates of the sturgeon. Virchow in the first instance believed that, in accordance with his views on the nature of the connective tissues, he had in these corpuscles isolated the proper cells of bone; and their isolability in such experiments was supposed to depend upon the great resistance of an imaginary cell membrane to the action of hydrochloric acid. We now know, however, that the isolation of these structures can be effected, not only in dry bones, as Virchow already knew, but also in bones which have been long macerated or treated with strong alkalies,|| and therefore under conditions which would destroy all soft tissues; hence we must admit, that in these experiments a peculiar dense and resistant layer of the matrix of the bone itself is

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* *Ueber ein plasmatisches Gefässystem in allen Geweben insbesonders in Knochen und Zähnen*, "On the presence of a Plasmatic Vascular System in all forms of Tissue, but especially in the Bones and Teeth." Hamburg, 1846.

† *Würzburger Verhandlungen*, Band i., 1850, p. 193.

‡ *Archiv für Pathologische Anatomie*, Band xviii., p. 70.

§ *Idem*, Band v., pp. 179 and 181.

|| E. Neumann, *Beiträge zur Kenntniss des normalen Zahnbein und Knochengewebes*, "Essays on healthy Dental and Osseous Tissue." Königsberg, 1863, p. 42.

isolated, which forms the wall of the cavities representing the form of the so-called bone corpuscles and their processes. The observations of Kölliker* and of Neumann† have an important bearing on this explanation, since in a similar series of experiments they frequently obtained isolated tubules, simulating the form of the Haversian canals. The question, what is the nature of the contents of these cavities during life? is, as thus broadly stated, not easy to answer.

According to a very recent communication, Klebs‡ has convinced himself that their contents in the older bones, even when quite fresh, is of a gaseous nature. He rests his assertion especially upon the dark appearance the bone corpuscles present by transmitted light, either in bones examined in the fresh state or under water; secondly, because by means of an air pump a large quantity of gas can be obtained from the bones; and lastly, because exposure to a solution of potash, which effects the absorption of the contained air (CO_2), renders the corpuscles transparent.

The bone corpuscles appear to be destitute of air in those bones only which are in contact with soft parts, or in fœtal bones; in point of fact, it is not difficult to demonstrate in many instances, that cell-like structures containing nuclei occupy the lacunæ of bone.§

For observations of this nature the large lacunæ of embryonic bones are well adapted, as are also those which are found in the younger layers of bone that lie immediately subjacent to the periosteal connective tissue investing the bones. Good results may be obtained from bones decalcified with weak acids (chromic acid, or a mixture of this with a little hydrochloric acid), especially if thin sections are tinted with carmine. On the other hand, it is difficult, even after this procedure, in the case of old bones, to recognise with certainty

* *Mikroskopische Anatomie*, p. 83.

† *Loc. cit.*

‡ *Centralblatt für die medicinische Wissenschaften*, 1868, p. 61.

§ Donders, Mulder, *Versuch einer physiologische Chemie*, p. 595. Kölliker, *Mikroskopische Anatomie*, Band ii., p. 297. Rouget, *Journal de la Physiologie*, 1858, p. 764. Beale, *loc. cit.*, p. 128.

either cells or their remains in the granular masses which occur in the lacunæ, and which were long ago observed by Schwann in decalcified bones.

Sharpey* has described certain fibres which come into view, if we attempt to isolate the lamellæ of a decalcified flat or long bone, as constituting a special morphological constituent of osseous tissue. They run in planes which lie nearly perpendicular to the surface of the lamellæ, and appear as pointed processes projecting from the surface of those lamellæ that have been torn away from their attachments; whilst in the adjoining lamellæ the foramina may be recognised from which these so-called Sharpey's or perforating fibres have been withdrawn. As H. Müller† showed, they occur in man in the bones developed in periosteum, and may there attain a length of as much as three millimeters, whilst their thickness varies from 0·002 to 0·005, sometimes even to 0·015 millimeters.

The perforating fibres are calcified rods, which, prior to the formation of the bone lamellæ they traverse, extend as bridges between the embryonic bone and the surrounding connective tissue, through the formative layers of the bone lamellæ; with increasing thickness of the lamellæ they first elongate and then calcify. When a portion of these fibrous bundles remains uncalcified, they form, according to H. Müller, when the bone is dried, the perforating tubes described by Tomes and De Morgan.

Kölliker‡ has called attention to the wide distribution of the perforating fibres, especially amongst Fishes.

Development of Bone.—Embryological investigation shows that almost the entire bony skeleton of vertebrate animals is developed from a cartilaginous skeleton which is laid down at an early period. This was originally held to be the mode of development of all bones, till Sharpey and Kölliker demonstrated that several of the cranial bones originated directly from connective tissue. These constitute the investing bones of the primordial skull. It has now been known for a con-

* Quain's *Anatomy*, sixth edition.

† *Würzburger naturwissenschaftliche Zeitschrift*, Band i., p. 296.

‡ *Ibid.*, Band i., p. 306.

siderable time that both kinds of bone, those developed in cartilage (primordial bones), as well as the investing bones (secondary bones), when once formed, receive fresh accessions of osseous tissue from the periosteal connective tissue, and that they thus increase in thickness. Virchow* first pointed out that in these cases the osseous tissue is developed from connective tissue in the same way as in the development of secondary bones.

According to these different processes, three separate modes of development of bone may be differentiated, the intra-cartilaginous, the intra-membranous, and the periosteal; but we shall see that in all these cases the osseous tissue originates in an essentially similar neoplastic formation (osteogenous substance), and also that the connective-tissue-like deposit preceding the formation of the several bones probably in all cases proceeds from the same germs; in short, that the above-mentioned differences refer to the place where the bone develops, and to the presence or absence of cartilage, but that the process of osteogenesis itself is essentially the same in all.

In those cases where the form of the future bone is more or less distinctly defined in the embryonic cartilaginous skeleton, it may easily be supposed that the matrix of the bone originates in a metamorphosis of the matrix of the cartilage, and the lacunæ and corpuscles either as outgrowths of the cartilage corpuscles, or by the formation of layers of secondary deposit, traversed by porous canals, occurring in the supposed membrane of the cartilage cells. In regard to the formation of the larger medullary spaces, we must admit a process of absorption of the cartilage, or of the young bone developed from it, with coincident development of the contained material. These statements, which were first advanced as a matter of opinion by Schwann† and Henle,‡ have obtained general acceptance, and for a long time were believed, in Germany, England, and France, to be in accordance with the direct

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* *Archiv für Pathol. Anat.*, Band v., p. 36, *et seq.*

† *Mikroskop. Untersuch.*, etc. Berlin, 1839, pp. 35 and 115.

‡ *Allgemeine Anatomie*, 1841, p. 831.

observations which had been made in ossifying cartilage.* This was especially the case in Germany, Kölliker† having employed rachitic bone as a microscopic object where the mode of conversion of cartilage corpuscles into bone corpuscles, described by Schwann as being analogous to the formation of dotted vegetable cells, may really be distinctly followed; and recently Lieberkühn‡ has investigated the normal ossification of cartilage in a series of papers, and has sought to represent the principal facts in accordance with the statements above made in regard to the transformation of cartilage into bone. Another mode, which has proved to be the correct one, notwithstanding that only a few§ were inclined to accept it, was proposed by H. Müller|| in 1858. It was further pursued by other observers,¶ and has led to the establishment of the essential facts to be now mentioned regarding the ossification of cartilage.

The ossification of those parts of the skeleton which are originally cartilaginous, proceeds, as is well known, from certain points, called points or centres of ossification. In these there appear in the first instance tubes (cartilage canals) filled with a soft cellular mass, into which blood-vessels, springing from the perichondrium, may be traced (medulla of cartilage). These canals lead to those parts where, in consequence of the deposition of the salts of lime in the matrix of the cartilage, the white appearance and firm consistence of bone are first observable, and form large irregularly dilated spaces, which are also

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* See for the historical details of the subject the paper by H. Müller in the *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 147, *et seq.*

† *Mittheil. der Zürich Naturforsch. Gesell.*, 1847, Nos. 11 and 12; and Froriep's *Notizen*, 1848, p. 120.

‡ Reichert and Du Bois' *Archiv*, 1862, p. 702; 1863, p. 614; 1864, p. 598; 1865, p. 404.

§ E. H. Weber, Ausg. v. Hildebrandt's *Anatomie*, 1830, p. 334, u. d. f. Sharpey, Quain's *Anatomy*, fifth edition. Bruch, *Denkschr. d. schweiz. Naturf. Ges.*, Band xi. Baur, Müller's *Archiv*, 1857, p. 347.

|| *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 145.

¶ Gegenbaur, *Jenaische Zeitschrift für Medicin und Naturwissenschaften*, 1864, p. 343; 1866, pp. 54 and 206. Landois, *Centralblatt für die medicin. Wissenschaften*, Berlin, 1865, Nos. 16, 18, and 32; *Zeitschrift für wissenschaftliche Zoologie*, xvi., p. 23. Waldeyer, *Ueber den Ossificationsprocess*, *Archiv für mikroskopische Anatomie*, Band i., p. 354.

filled with medullary matter containing blood-vessels. These spots, traversed by dilated canals, lend support to and confer firmness upon the remains of the cartilage, which has now in great part apparently undergone absorption, and is thoroughly impregnated with granular deposits of lime. In the neighbourhood of these spots the cartilage appears transparent and composed of large clear cells separated from one another by only a small portion of matrix. When a more careful examination is instituted, it is observable, however, that the limits of the cavities filled with medulla, and the large-celled cartilage region, on the one hand, and the limits of the calcified trabeculæ and the large-celled cartilage region on the other, do not coincide ; for the calcified portion may be followed beyond the limits of the medullary spaces, and terminates in the form of fine processes in the larger trabeculæ of the matrix of the still unpenetrated cartilage. The cells at the limits of the latter appear to occupy the tubular extremities of the calcified tissue, and there first come into contact with the medulla. Such are the processes in cartilage that precede the formation of bone. Osseous tissue is only developed in those parts where medullary substance has been first formed, and, indeed, upon its surface, being superimposed upon the previously calcified cartilage. In regard to this point, however, a fuller description will hereafter be given. It is not difficult to see these phenomena in the centres of ossification of the short bones, or in the diaphyses of the long bones. The centres of ossifications of the epiphyses which appear at a later period are also exceedingly well adapted for observations of this kind. The embryoes from which the preparations are made ought previously to be macerated in chromic acid, or still better, in Müller's fluid. The most instructive specimens are furnished by keeping the preparations for a somewhat longer time in the latter fluid till they can be cut with facility, and then staining them with carmine.

The changes described gradually extend from the centre of ossification into the adjoining cartilage. Longitudinal sections through the diaphyses of fœtal bones, which display the margins undergoing ossification, are best adapted for microscopic investigation. The appearances presented by such a longitu-

dinal section, if it contains all the parts undergoing change from the still unaltered cartilage to completely formed bone, are the following (fig. 12). Immediately below the cartilage exhibiting the characters of fœtal cartilage, as it appears previously to

Fig. 12.

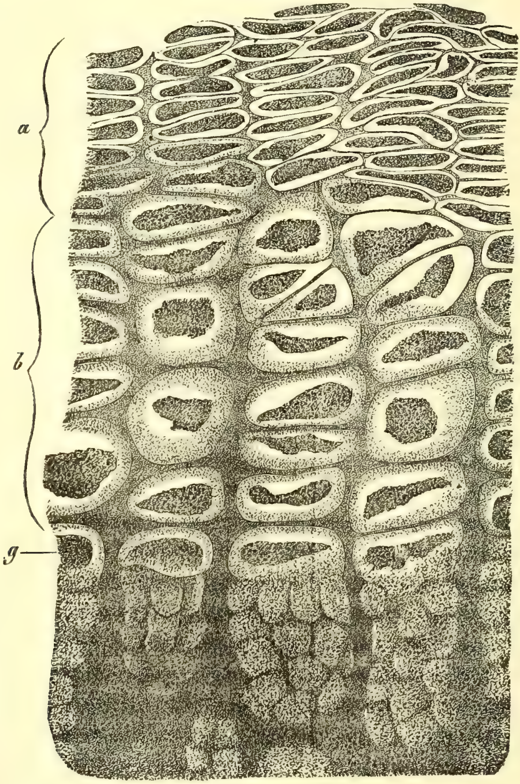

Fig. 12. Longitudinal section carried through the line of ossification of a tubular bone. From a human embryo.

ossification, there follows a layer of cartilage (a) in which the cells lie more closely compressed together, and present a definite arrangement. They form longitudinal rows. In these rows the cells appear as plates flattened in the direction

of the long axis of the bone, superimposed upon one another, so that a transverse section made from this region presents some similarity to that of the free surface of the articular cartilages, or that exhibited by other cartilages in the layer immediately beneath the perichondrium. These long rows of flat cells are further characterised by the circumstance that they are often clavate, and intercalate with one another alternately, with their pointed extremities directed in opposite ways.* It is moreover not difficult to convince one's self that these rows of cells originate in continuous processes of fission; and in regard to this point the preparations are very instructive that were examined and described by Aeby, showing that the club-shaped cells develop from the transverse fission of elongated cells, the daughter cells becoming placed alternately one above the other. The several long rows of flat cells are not all arranged at equal distances from one other, but are divided into variously sized vertical groups by strong trabeculæ of the matrix.

To the well characterised region of flattened cells, arranged in vertical rows, there succeeds near the line of ossification a second region (*b*), in which clear and remarkably large cells containing beautiful spherical nuclei are found. The larger size of these cells, in comparison with those contained in the region just described, is to be attributed chiefly to the increase of the diameter coinciding with the longitudinal axis of the bone. This region contains in the same area a much smaller number of cells than even the primary cartilage lying over the region where they are arranged in vertical rows. Examined with the naked eye, the region of large cells seen in longitudinal section in fresh fœtal bone appears clearer and more transparent than any other part. This region presents a great similarity to that stage of fœtal cartilage in which the cells are still capable of being easily isolated.

Between the large transparent cells such strong trabeculæ of the matrix alone intervene as run parallel to the longitudinal direction of the bone, and between which the cells lie in single or more frequently in multiple rows. Where these trabeculæ

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* Aeby, *Zeitschrift für rationelle Medicin*, 3 R., Band iv., p. 38, u. d. f.

are absent, the cells appear to be in direct contact with one another. Even then, however, when the cells have become somewhat shrivelled, a very delicate structure may be distinguished, formed by the presence of small quantities of the matrix intervening between each of the vertical rows. The septa intermediate to the cells in the latter case are arranged like the steps of a ladder (see the illustration) between the adjoining longitudinal trabeculæ. Still more internal to the region of large cells, the thicker vertical trabeculæ become the seat of the deposit of the lime salts, in the form of small granules or confused masses on their internal surface, and at the same time they become somewhat thicker. We then reach the region of calcified cartilage, which, according to H. Müller,* usually precedes the true process of ossification. A very beautiful mode of supplementing the images hitherto only seen in longitudinal section, and which have been best described by Waldeyer,† is that by which transverse sections are examined that are successively carried through the several regions above described.

The appearances presented by transverse sections of the calcified cartilage are especially worthy of notice. In these, calcified rings surrounding one or several of the large cells, and characterised by their granular or cloudy appearance, come very distinctly into view. If the transverse section approximates nearer to the bone, the calcified rings increase in thickness, and still lower down the cells which occupy the calcified rings become smaller, more numerous (fig. 13), and more strongly granular. Beneath these cells we find masses of protoplasm often of considerable size, containing two or more nuclei, together with a great number of small nuclei. The many-nucleated cells have been rightly associated by Gegenbaur‡ and Waldeyer§ with the myeloplaxes described by Robin.‖ The selection of successively lower planes for the transverse section thus leads from the large-celled region, the calcified

* *Loc. cit.*, p. 157.

† *Loc. cit.*, p. 359, v. Taf. 22, fig. 2.

‡ *Loc. cit.*, p. 349.

§ *Loc. cit.*, p. 362.

‖ *Journal de la Anatomie, de la Physiologie*, Tom. i., p. 88.

rings remaining without essential change, to a plane in which proliferated cells appear between the calcified trabeculæ. This also immediately becomes evident if we return to the examination of a longitudinal section.

The appearance presented by a longitudinal section is further rendered very remarkable by the circumstance that the elongated spaces bounded by the above-described calcified trabeculæ, suddenly, at a tolerably well-defined limit (*g*, fig. 12), change their contents from large cartilage cells to a material of a different nature. This consists of granular cells that lie closely

Fig. 13.

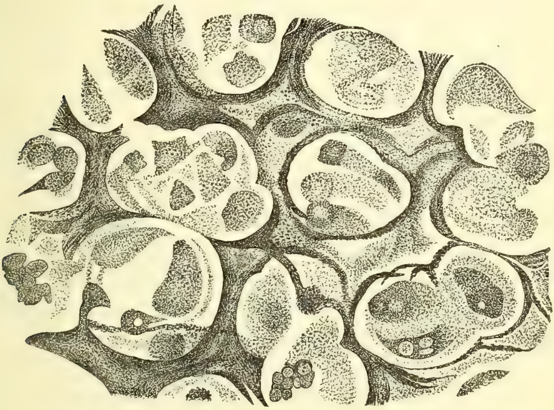

Fig. 13. Transverse section through fœtal cartilage in which ossification has commenced.

compressed against the cartilage. These cells are provided with a variable number of longer or shorter processes, which, however, can only be well seen in preparations that have been teased out with needles, or pencilled out with a brush. If we follow up the trabeculæ surrounding these masses in the direction of the cartilage, we shall see that the granular cells, accumulated where the cartilage commences, form an epithelium-like layer investing the surfaces of the expanded prolongations of the vertical trabeculæ, whilst the middle part of the contained mass is occupied by delicate fusiform or stellate cells, amongst

which, however, small roundish coarsely granulated cells are distributed. In this last tissue well-developed blood-vessels are clearly visible.

Thus in the cavities of calcified cartilage there appears in the first instance a new soft material composed of numerous cells, of which the superficially situated are differentiated from those that occupy the interior.

The question now arises, from whence do these tissues originate? It is to be remarked that the limits between the large-celled region of the cartilage, and the subsequently formed contents of the spaces bounded by the calcified trabeculæ, are very sharply defined in all the preparations I have examined. I have never been able to discover any transitional stages between the large clear cartilage cells and the dark coarsely granular cells which suddenly make their appearance. Such transitional stages might, however, be expected to occur frequently if the cartilage cells constituted mother cells, giving origin to those of the medulla by fission. However high, therefore, may be the authorities by which the latter view is supported, I must still doubt its accuracy. It is indeed conceivable that processes of division may here occur with such rapidity as to be concealed from the eye of the observer, and thus lead us to grant the development of the medulla from the cartilage cells, as a convenient theory, though unsupported by direct observation. We are certainly, however, not compelled to admit this view, since there is no difficulty in supposing the medulla to shoot into the cartilage from the same surface as that from which the blood-vessels emanate. This last view is especially supported by the circumstance that, as we shall see, an analogous productive activity must necessarily be attributed to the medulla, and will hereafter be traced in it.

The productive activity of the cartilage cells appears to me to cease at the limits of the flat-celled region. The large vesicular cells which extend from this point to the plane of ossification may frequently be seen where the medulla commences, in a state of finely granular atrophy, similar to that of the cartilage matrix itself, so that only the remains of these cells are found in the medulla.

The view here given at length must not be confounded with

the statements made by Henke,* respecting the origin of the cartilage elements at the plane of ossification, according to which even the vertical rows of cells contained in the medullary spaces are formed at the expense of blood corpuscles that have escaped from the vessels.

We have already pointed out that coincidently with the change that occurs in the nature of the material occupying the interspaces of the calcified trabeculæ a differentiation of its constituent cells may be observed to take place into an outer and an inner layer.

The granular cells of the outer layer were first described by Gegenbaur,† who applied the term *Osteoblasts* to them, whilst he considered the more transparent internal tissue to be the proper medulla in an early stage of development. The osteoblastic layers are found in the cavities already described (primary medullary spaces), sometimes forming thin and sometimes thicker layers, interposed between the remains of the original cartilage on the one hand, and the vascular medulla on the other.

The formation of the osteoblastic layer constitutes the immediate precursor of true osseous tissue. The latter occurs in the walls of the primary medullary cavities, at some distance from the margin of the cartilage, and when first seen constitutes a thin, lustrous, highly refractive lamella, in which the peculiar stellate form of the bone corpuscles is already visible. Wherever this tissue is formed, osteoblasts have previously been deposited in layers, and just as in the first instance the remains of the trabeculæ of the calcified cartilage, so at a later period the young bony tissue deposited on the surface of these is again covered by a layer of osteoblasts separating it from the medulla.

All the peculiarities above described, with the above-mentioned exception of the relation of the cartilage cells to the medulla, may be traced with perfect accuracy.

It is more difficult to ascertain the relation of osteoblasts to newly formed bone.

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* *Zeitschrift für rationelle Medicin*, 3 R., Band xviii., p. 61.

† *Loc. cit.*, p. 360.

Gegenbaur supposes the osteoblasts to form a hardening secretion, in which they are subsequently themselves enclosed, appearing in the form of the stellate bone corpuscles. Waldeyer has drawn attention to the difficulties of this explanation, and has sought to show that the osteoblasts are constantly converted into bone in a lamellar fashion, whilst new layers are constantly being differentiated from the medulla. In undergoing this change the osteoblasts assume a smoother and more homogeneous appearance, and, whilst their nuclei break down and vanish, become hardened into the matrix of bone; in some of them, however, only the external portions undergo this fusion and calcification, the inner portion with the nucleus remaining as bone cells enclosed in a stellate cavity. The latter explanation corresponds with much greater exactness than the former to the facts that have been observed.

Before discussing this subject further, we shall now proceed to show that the formation of bone in periosteal tissue and in investing bones occurs under the same conditions as those of which we have acquired a knowledge when considering intra-cartilaginous ossification. In reference to the latter it must still be remarked that although the exposition given above has been especially derived from the examination of human embryoes, it has also been observed in allied animals.

In describing the processes taking place at the ossifying surface of the diaphyses, we have already become acquainted with those which determine the increase in length of the tubular bones. Their *increase in thickness* is dependent upon the processes we are now about to describe. Grew* and Havers† were the first to point out that a deposit of new bone takes place upon that already formed from the periosteum, but it was the researches of Du Hamel‡ that led to the general recognition of the fact.

In the development of the tubular bones, the process of periosteal ossification may even precede the intra-cartilaginous.

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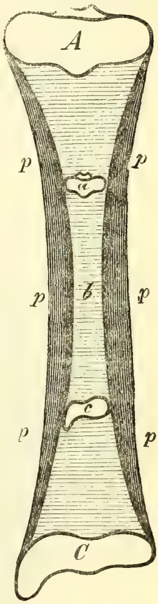
* *English Academy*, 1681.

† *Osteologia*, etc. Frankfurt and Leipzig, 1692.

‡ *Mémoires de l'Academie de Paris*, 1742, p. 354; 1743, pp. 87, 111, and 288.

In such cases the cartilage, either in a pure state, or perforated by canals, and calcified, and in the preparatory stage of intra-cartilaginous ossification, becomes enclosed in a tube of osseous tissue.* In certain animals, medullary substance replaces cartilage in the middle portion of the bone; whilst in other animals, and also towards the apophyses of the bones in the former instances, a few intra-cartilaginous bony trabeculæ are developed, which become altered to the periosteal tube. In a few cases, as for example in sections of the tubular bones of the extremities of the adult Proteus, we find an osseous tube composed of a few periosteal lamellæ, the cavity of which is filled with true cartilage that has undergone calcification.

Fig. 14.



An easily intelligible diagram, showing intra-cartilaginous and periosteal ossification proceeding together, as occurs in the formation of the long bones of the higher vertebrata, is exhibited in the adjoining figure (fig. 14), by H. Meyer;† *a b c* indicate the bone of an infant; A *b* C the form which the bone of the adult acquires by intra-cartilaginous growth, whilst its increase in breadth results from the periosteal deposit *p*. The ossific capacity of the periosteum causes a reproduction of bone to occur if the latter be resected from its investing periosteum.‡ Upon this circumstance depend the osteo-plastic processes that have been observed after the transplantation of excised portions of periosteum, and which are especially active in young animals, and to some, though a smaller extent in adults.§ The peculiar histological processes occurring in periosteal ossification have been fully discussed by Virchow, and more recently

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* Dugés, Rathke, Bruch, Reichert, H. Müller, *loc. cit.*, p. 193.

† Müller's *Archiv*, 1849, p. 292.

‡ Heine, Gräfe and Walther's *Journal*, 1839, p. 513, and many recent observers.

§ Ollier, *Journal de la Physiologie*, Tom. ii., pp. 1 and 169.

by Gegenbaur, Waldeyer, and Landois, in the works above mentioned. The processes are more simple in animals where successive lamellæ only are deposited, but more complicated when Haversian canals are developed, with their concentric systems of lamellæ.

We shall in the first instance discuss the processes which occur in the latter case, and for this purpose a transverse section carried through one of the bones of the forearm of a human embryo at the fifth month, invested with its periosteum, may be advantageously studied (fig. 15). With low microscopic powers we obtain from this the very instructive appearance which is diagrammatically represented in fig. 15. The dia-

Fig. 15.

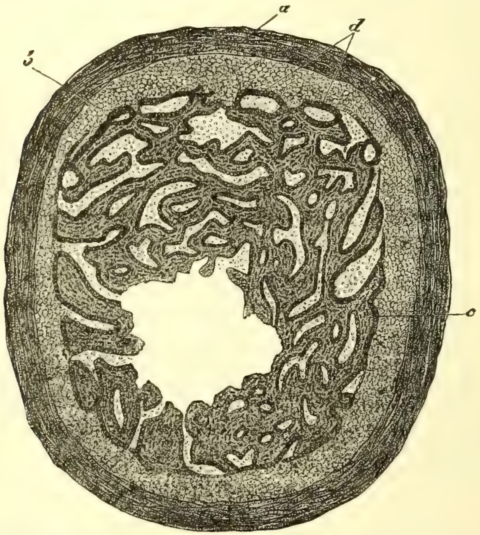

Fig. 15. Transverse section through one of the bones of the forearm of a human embryo, at the fifth month. (Half diagrammatic.)

grammatic character of the illustration, however, relates only to the tissue elements introduced into it. The dimensions of the several layers being correctly indicated.

A homogeneous smooth lamina may here be seen in the first place constituting the outer layer of the periosteum, consisting,

as appears from its examination with high powers, of decussating fasciculi of connective tissue divided in various directions in the section. Between the fibrillæ fusiform cells with elongated nuclei are distributed. To this external layer of the periosteum succeeds a tolerably broad internal layer *b* (Cambium),* which with low powers is distinguished by its containing a large number of small round bodies that appear to be imbedded in the meshes of a fine plexus, and confer upon it a granular aspect. If we examine these layers separated from one another under high powers, and combine therewith the results obtained from the investigation of preparations teased and pencilled out, we shall observe in the first place that the granular appearance depends upon the presence of small roundish nucleated cells. The cells give off a variable number of fine processes from their periphery, which join the reticulum; the latter possesses a structure which it is difficult to unravel, for we do not find in it the well-developed stellate cells present in the reticulum of the lymphatic glands, but flattened cells that are finely granular in the portion lying next to the nucleus, and at various points, but frequently only at the two opposite poles, give off long homogeneous processes. In very many instances the isolated cells become continuous at their periphery with a fine trabecular trellis-work of wing-like form connected with other fine and smooth trabeculæ traversing the reticulum.

On the internal surface of the second layer of the periosteum which we have just described, there follows a third layer *c*, which contains large granular cells exactly comparable to the above-mentioned osteoblasts, and forms an epithelial covering continuous with the periosteal investment of the bony trabeculæ. By teasing out the specimen with needles, it may be demonstrated that the apparently spherical cells are here also provided with numerous fine homogeneous processes, which on the one hand penetrate into the already described reticulum, or on the other hand extend to the surface of the bone, into the substance of which they pass without interruption.

The cellular investment of the osseous trabeculæ is, however,

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* Billroth, *Archiv für klinische Chirurgie*, Band vi., p. 723.

not continuous, since between the separate granular osteoblasts the somewhat expanded processes of the before-mentioned reticulum penetrate and proceed directly to the surface of the bone, into the matrix of which they pass without apparent interruption. In correspondence with the larger size of the osteoblasts, the meshes of the reticulum of bone are likewise enlarged.

Such are the appearances presented by a transverse section in which fully formed bone, layers of osteoblasts, and small-celled and fibrillar periosteal layers immediately succeed one another in parallel series.

This, however, can be observed only in a few places. The external form of the transverse section shown in fig. 15 is conformed to the shape of the external and internal limits of the fibrillar portions of the periosteum. The internal surface of the bone everywhere invested with osteoblasts is, on the other hand, irregularly bulged and dentated, whilst the arcuate boundaries of the cavities occurring in the bone project towards the periosteum. From the arches of the completely developed bone other arches spring, which, exclusively composed of osteoblasts, are directly continuous with the osteoblasts investing the bony trabeculæ. The last-named arches are either entirely closed externally, forming completely differentiated rings of osteoblasts, or we may observe two arched processes inclined to one another, constituting the commencement of a future ring. These incomplete arches then enclose a part of the already described small-celled second layer of the periosteum, the enclosed and the unenclosed portions being continuous through the orifice left in the crown of the arch, and in the first instance presenting identical characters. We have thus acquired a knowledge of the first formation of the Haversian system and canals, as well as of the medulla primarily contained in the latter. In passing from without inwards we may recognise all stages of transition from the first formation of the projecting osteoblastic arches, and from the first incomplete arches projecting from the bone, and closed only by an osteoblastic layer, to the completely closed lamellæ of bone. All these newly formed rings and arches of bone are invested on their inner surface with osteoblasts, and upon their external

surface also, especially where they are in contact with the periosteum. The tissue enclosed by the newly formed bony arches soon becomes more transparent, highly vascular, and then contains small roundish cells which appear granular, together with others that are more transparent, elongated, and fusiform, resembling those which are met with in young connective tissue. In the mode illustrated by the example we have adduced, the process of formation may be followed in the later stages of development, during the period of increase of the bone in thickness.

Since the great medullary cavity occurs as a secondary formation in the tubular bones, in consequence of a great part of the bone developed by intra-cartilaginous ossification having undergone re-absorption, we find in adult bones that the medullary cavity in the middle portion of the shaft is bounded for the most part only by the intercalated or Haversian systems of bone which have been formed by periosteal osteogenesis.

As in the intra-cartilaginous mode of ossification, so also in the periosteal form, a continuous layer of osteoblasts may be observed to constitute the immediate precursor of the formation of the osseous tissue.

It still remains to be noticed, that, in transverse sections made as before, strong fibrous bands may be followed, pursuing a radiating course through all the layers of the periosteum, from the exterior to the bony trabeculæ; these are continuous with the fasciculi of the outer layers of the periosteum, appear to be quite independent of the rings and arches of osteoblasts, and are to be regarded as the earliest condition of the perforating fibres of Sharpey.

If we examine the longitudinal section of one of the long bones of an aborted embryo or very young child, in the same way that we have already examined the transverse section, we shall see stretching over spaces of considerable extent in the periosteum, near the surface of the bone and imbedded in the small-celled layer of the periosteum, a layer of well-defined osteoblasts, arranged longitudinally in a striated manner, in which the processes that take place are less distinctly visible than in transverse sections, and, indeed, become intelligible only by comparison with the latter. The appearances presented by such longitudinal sections are, however, very similar

to those which are obtained from the early stages of development of the so-called investing bones.

The ossification of the investing bones, the so-called *intra-membranous ossification*, was first distinguished from the intra-cartilaginous by Nesbitt,* and subsequently by Sharpey.† The description of intra-membranous ossification given by Sharpey was substantiated by Kölliker, and in consequence obtained general acceptance. The finer details of this mode of ossification may be found in the recent observations published by Lieberkühn‡ and Waldeyer.§

The expanded portion of the occipital bone, the parietal and frontal bones, the squamous portion of the temporal bones, the ossa Wormiana, and the facial bones are all developed in membrane. The clavicle was included in the number of these bones by Nesbitt and Bruch, but incorrectly, as was shown by H. Müller|| and Gegenbaur.¶ The development of those bones which are not formed in cartilage proceeds, however, like them, from one or from a limited number of points. The tissue in which these bones originate exhibits a great similarity to that which has been already described as the second layer of the periosteum, or as constituting the young medulla within the rings of well-defined osteoblasts. In this tissue there first appear at the points from which the ossification commences, small thin trabeculæ, which unite in a plexiform manner, and this differentiation of tissue progressively extends in a radiating direction. The spaces enclosed by the anastomosing trabeculæ are wider towards the periphery than at the point from whence the ossification commenced. Towards the periphery the trabeculæ are also thinner, and form finely pointed and radially directed processes, and after assuming this arrangement become calcified and converted into bone. If we examine such trabeculæ before they have undergone ossification, it will be seen that they

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* *Osteogeny*, etc., translated by J. C. Greding. Altenburg, 1753.

† Quain's *Anatomy*, by Quain and Sharpey, fifth edition.

‡ Reichert and Du Bois' *Archiv*, 1864, p. 610.

§ *Loc. cit.*, p. 368.

|| *Loc. cit.*, p. 201.

¶ *Jenaische Zeitschrift*, 1864, p. 1.

consist of numerous cells, elongated in accordance with the long axis of the trabeculæ. These cells appear strongly granular in their thicker median portion, and contain a round nucleus. They resemble the osteoblasts found elsewhere, but are elongated to a still greater extent in one of their axes. Between these cells with their interlacing processes, fibres extend, either singly or in small bundles, in association with which the processes of these cells run, so that the several trabeculæ present collectively the appearance of connective tissue at a certain stage of its development. At a period immediately succeeding the formation of this fibro-cellular material constituting the rudiment of the secondary bones, we may

Fig. 16.

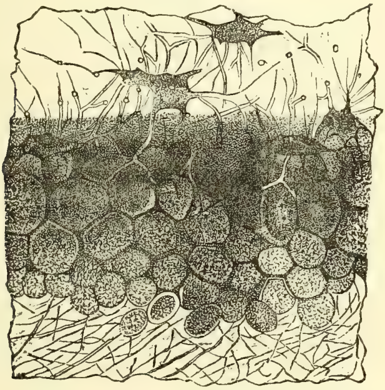

Fig. 16. Bone trabeculæ with osteoblastic layer, from the parietal bone of a human embryo, at the fifth month.

trace in the most beautiful manner, in preparations which have been teased out, how the whole deposit calcifies and acquires the character of osseous tissue. Each newly formed trabecula of bone is invested on its surface with a layer of osteoblasts, and in proportion to the increasing thickness of the trabeculæ the investing layers of osteoblasts assume the character of an epithelial layer (fig 16), as it presents itself in the primary medullary spaces of the long bones, or in the material in which the Haversian canals are about to form. The

trabeculæ of a secondary bone, proceeding from different centres of ossification, unite with one another at a later period. They form broad transverse trabeculæ, parallel to the surface of the bone on which new layers are deposited, causing the bone to become thickened, as in the periosteal increase of bones developed from cartilage.

When we thus follow the three above-named modes of development of osseous tissue, it is seen that we meet only with variations that gradually pass into one another.

In the case of intra-cartilaginous ossification, the substitution from the first of a new tissue for the cartilage which subsequently calcifies, removes the difficulty of explaining the molecular difference between the matrix of cartilage and the organic matrix of bone which was formerly experienced, when the impregnation of cartilage with salts of lime was regarded as the essential condition of the ossifying process.

There further occurs a complete agreement between the origin of the first rudiments of true bone and the primary layers by which growth is effected. In reference to the latter, it is found that they only partially succeed one another in a centrifugal direction, leading to a change of form in the bone, whilst they are chiefly superimposed centripetally towards the cavities which were bounded by the first deposits, leading probably in all instances to a relative increase or diminution of the sclerosed as well as of the soft parts contained in a given area. We do not possess any macroscopic observations which tend to the supposition that, in bone once formed, growth may occur by intus-susception. The microscopic observations instituted in reference to this point are open to various interpretations, and we shall only remark here that objections have been recently raised against the well-known experiment of Hunter, negativing an interstitial increase of bone, because two orifices made in the shaft of the long bone of a young animal did not retreat from one another.

We have seen in our microscopic investigations how intricate the relations are in regard to centrifugal and centripetal deposition of new bone, and how the formerly described periosteal development of the complex long bones, in which the greater part of the intercalated and investing lamellæ, and the

most external Haversian lamellæ originate apparently by centrifugal deposition, whilst the internal Haversian lamellæ originate in centripetal deposit.

If sections are made of growing bones decalcified with chromic acid, or if bone be macerated in Müller's fluid, which however does not facilitate their section, and are then rubbed down with this fluid and treated with carmine, the osteoblastic layers and the immediately adjacent youngest layer of bone acquire an intensely red colour, whilst the remainder of the osseous tissue, with the exception of the bone corpuscles, remains uncoloured. We thus obtain specimens very similar to those made from the bones of animals fed for a short time with madder, which have been described and depicted by Tomes and Hassall.*

It is well known that it has been sought to draw some definite conclusions respecting the process of absorption and regeneration of bone, from the observation of the laminated coloration of the osseous tissue occurring after the use of madder, on the ground that such coloured parts represent the most recently formed layers.

It is well worthy of notice that the experiments with madder first instituted by Du Hamel,† and repeated at a later period by Flourens,‡ at a time when very little was known respecting the histological process of ossification, and which were certainly unjustly brought into discredit by Gibson,§ have again been recently taken up by Lieberkühn. The above-mentioned analogies, and the more delicate histological relations occurring in the formation and resorption of osseous tissue, still require to be subjected to a systematic investigation.

Contents of the Bone Cavities.

The medulla which occupies the central cavity, and the large medullary spaces especially found in the fully developed long bones, is composed of a delicate connective tissue traversed by

* *Loc. cit.*, plate 30, fig. 6.

† *Mémoires de l'Academie de Paris*, 1742, p. 354; 1743, p. 138.

‡ *Annales des Sciences Naturelles*, série 2, xiii., p. 103.

§ Meckels' *Archiv*, Band iv., p. 482.

vessels, and containing numerous fat cells, to which last its yellow colour is due (yellow medulla). This fatty medulla cannot in any way be compared with the above-described young medulla of bones in process of formation; it represents a stage of development of the former which has progressed in another direction, and no osteogenic activity can be attributed to it.

The medullary spaces of the spongy substance, on the other hand, contain a reddish mass traversed by numerous blood-vessels (red marrow), and presenting, with but few fat cells, a large number of granular cells similar to those that are found in the embryonic medulla. Amœboid movements occur in the cells of the bone medulla analogous to those seen in the colourless blood cells;* in the latter localities the large many-nucleated masses of protoplasm are found described by Robin† under the name of Myeloplaxes, and which are most abundant in the external layers of the medullary masses occupying the bone cavities. Bredichin‡ is of opinion that the colossal cells (Myeloplaxes) proceed from the bone tissue itself, *i.e.* from the bone cells with coincident absorption of the matrix, and that this conversion is continuous with the formation of medullary canals during the growth of the bone. As the different sized medullary spaces of the bone are continuous with one another, so do also the yellow and red medullæ gradually pass into one another. In the skeleton of birds many bone cavities morphologically comparable with the medullary cavity of other animals are filled with air instead of medulla.

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* Bizzozero. Rovida, *Wiener Sitzungsberichte*, Band lvi., p. 608; and *Centralblatt für die medicin. Wissenschaften*, 1868, p. 245.

† *Journal de l'Anatomie et de la Physiologie*, 1864, p. 88, plates 1, 2, and 3.

‡ *Centralblatt für die medicin. Wissenschaften*, 1867, p. 563, provisional communication.

CHAPTER III.

THE GENERAL CHARACTERS OF THE STRUCTURES COMPOSING THE NERVOUS SYSTEM.

By MAX SCHULTZE.

THE structural elements of the nervous system, speaking generally, are of three kinds. To the conduction of nervous influence the *nerve fibres* are subservient, which not only compose the nerve trunks, but also constitute an essential part of the substance of the central organs. At the peripheric extremities of the majority of these fibres peculiar *terminal organs* are found, representing the second structural element of the nervous system; whilst the third is formed by the peculiar structures situated at the origin of each fibre in the nerve centres. These are the *ganglion cells*. Our subject therefore is naturally divided into a consideration of

1. The nerve fibres.
2. The peripheric terminal organs of the nerves.
3. The centric organs of the nerve fibres.

THE NERVE FIBRES.

The nerve fibres form the chief constituents of all nerve trunks, in which they are mingled with connective tissue and blood-vessels; they also enter largely into the composition of the central organs, forming not only the whole of the white substance, but constituting a considerable portion of the grey matter. They are in part very simple, but in part also very complex structures, and there are consequently several varieties of them. The primitive nerve fibrils present the simplest form. These are the very fine threads which lie on the extreme verge of microscopic mensuration, and are only rendered visible

with powers effecting an apparent enlargement of from 500 to 800 linear. They are moderately frequent in the central organs and in the neighbourhood of the peripheric terminations. In such fibres as these no internal structure can be detected by the microscope. Their nervous nature is, however, placed beyond the possibility of question by their connection with

Fig. 17.

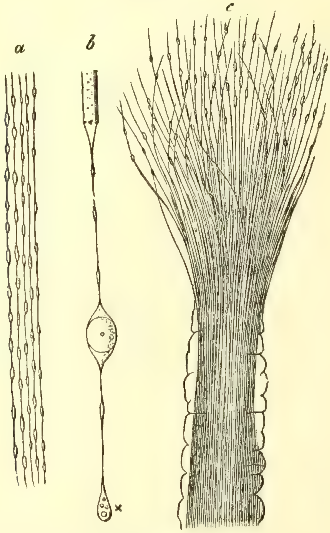

Fig. 17. Primitive nerve fibrils. *a*, from the nervous fibre layer of the retina; *b*, from the external granule layer of the retina, showing at *x* a larger varicosity, resulting from imbibition; *c*, from the olfactory groove of the Pike, showing a thick nerve fibre enclosed in a sheath, breaking up into fibrillæ.

ganglionic cells, and by the evidence of their issuing from thicker nerve fibres. When fresh, it is very difficult to isolate them, but this may readily be effected in preparations that have been carefully hardened. On treating the fibrils with watery solutions of different salts in certain degrees of concentration, and with solutions of chromic and perosmic acids, besides being hardened, they undergo during the first few hours a process of partial imbibition, occasioning the appearance of

varicose enlargements, having a more or less regular fusiform shape, and these subsequently, by further imbibition, increase in size and number until at length the fibre becomes unrecognisable and disappears.

A second kind of fibre very commonly met with in the central organs, is distinguished from the foregoing by its greater thickness. Such fibres are very delicate, transparent, and perishable, of albuminous composition, and only isolable for short tracts. Their diameter is very various, amounting only to a few micromillimeters. Speaking generally, they are the fibres which have been termed naked axis cylinders. The thicker they are the more easy is it to distinguish their internal structure. This presents a more or less well-marked longitudinal striation, resulting from a fibrous differentiation of the substance of the fibre, and from the presence in all probability of an interfibrillar finely granular material. It is most easy to discern that they are composed of fibrils in the thick-branched processes of the large centric ganglion cells, which Deiters proposed to call *protoplasmic processes,* a name for which I substituted the term *ramifying processes.** Moreover, the axis-cylinder processes even of these ganglion cells and other fibres of the central organs of the nervous system usually regarded as naked cylinders, and believed to run for considerable distances without branching, often present a distinctly fibrillar structure. Their fibrillar character is most distinctly visible at their origin from the ganglion cells, as shown in fig. 18 (at *x x*). I have applied the term "primitive-fibril bundles, or fasciculi," to this second kind of fibre.

Both kinds of fibres, the primitive fibrils and the fibrillar fasciculi, may become invested with a medullary sheath, as in the adjoining figure (at *a*), and thus become converted into a third form of nerve fibre, *the medullated.* The medullated fibres therefore consist essentially of two constituents, a cortex or sheath of medullary nerve substance, and an axial fibre or axis cylinder, which is either a primitive fibre or a bundle of fibrillæ. The medullary sheath forms a more or less thick

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* See Deiters' *Researches on the Brain and Spinal Cord,* Brunswick, 1865; and my Preface to his Book, pp. xv.—xvii.

investment around the axis cylinder, and consists of an oily substance containing protagon, and capable of powerfully refracting light. It gives to the nerves their characteristic dark strongly defined borders. Considering the great delicacy of the axis cylinder, and the perfectly fluid nature of the medullary sheath, the consistence of these medullated fibres cannot, it is obvious, be very great. In point of fact, the difficulty of isolating the medullated fibres of the nerve centres is quite as great as in the case of the naked axis cylinder. The isolation of unaltered fresh medullated fibres, obtained from the grey and white substance of the brain and spinal cord, can only be accomplished for short distances. The fibres break up into short pieces as soon as the preparation needles are used, partly in consequence of pressure and tearing, but partly also from the imbibition of fluid. Even when the more indifferent liquids are employed, these fragments of fibres rapidly undergo remarkable changes of form, developing knots and swellings on their surface (see fig. 19), and sometimes regular moniliform enlargements, though for the most part such enlargements appear only as irregular varicosities, giving a very characteristic appearance to the fibre. After a short time numerous spherical and short cylindrical curved masses separate from the medullary invest-

Fig. 18.

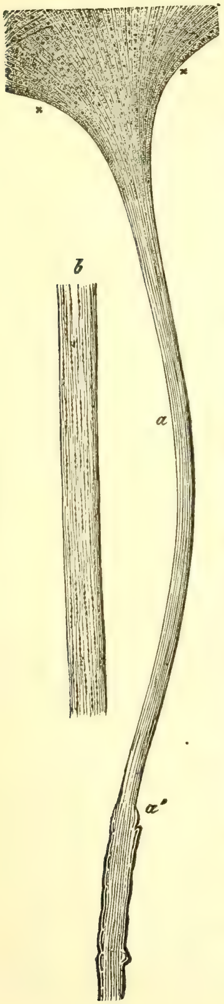

Fig. 18. *a*, axis cylinder, showing its fibrillar structure, at its upper part *x x* originating in a ganglion cell, and at *a'* becoming invested by a medullary sheath; *b*, naked axis cylinder from the dorsal region of the spinal cord of the Ox. The medullary sheath has been removed.

ment, or from the whole soft fibre, and swim freely in the liquid in which the preparation is contained, constituting the so-called myelin drops (*b*).

The medullary sheath, especially where it surrounds the axis

Fig. 19.

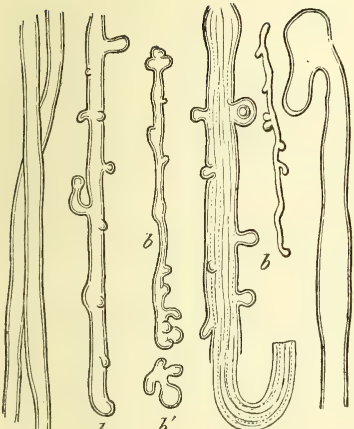

Fig. 19. Medullated nerve fibres destitute of the sheath of Schwann, recently removed from the fresh spinal cord. *a*, two unaltered fibres; *b b b*, fibres in which the medullary substance is swollen up by imbibition into irregular drops upon the surface; *b′*, a detached drop of the same nature (a so-called myelin drop); *c*, axis cylinder projecting from the medullary sheath.

Fig. 20.

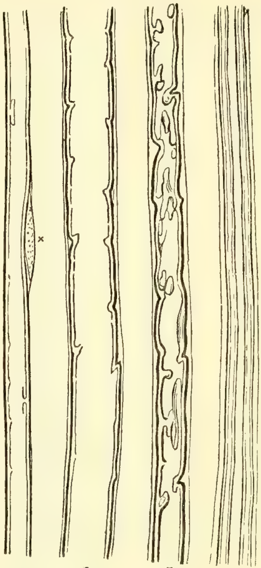

Fig. 20. Medullated nerve fibre invested by Schwann's sheath, quite fresh. *a*, with a nucleus in the sheath at *x*; *b*, a very broad fibre; *c*, two very delicate and closely approximated fibres; *d*, a fibre so changed by manipulation that it exhibits the so-called coagulation contours.

From the lumbar plexus of a Frog.

cylinder, as a somewhat thicker layer, changes after death, by what may be termed a kind of coagulation, into a granular semi-transparent mass. The changes proceed from without

inwards, affecting the homogeneity of the mass, and altering the originally transparent highly refractive fibre in a very peculiar manner (see woodcut 20, *d*). The change is accelerated by the addition of water, whilst it is delayed for many hours by immersion in solution of iodine in serum. The addition of a solution of perosmic acid hinders the coagulation of the medullary substance of the nerves in a similar manner, and moreover colours it of an inky black.

The medullated fibres of the nerve centres are imbedded in an extremely delicate tenacious spongy connective substance, the peculiar consistence of which preserves the fibres from injury, notwithstanding their softness, and the absence of any proper investing sheath.

The medullated fibres of the peripheric nerves, on the other hand, with the exception, perhaps, of those belonging to the optic and acoustic nerves, each possess in addition, and external to their medullary sheath, a special investment of connective tissue, constituting the so-called sheath of Schwann. This is either a structureless, perfectly transparent, delicate membrane, agreeing in its consistence and chemical constitution with the sarcolemna of muscular fibre, or consists of several layers of fibrillar connective tissue, and as in this presents nuclei scattered through its substance. If the membrane be very thin, the appearance of the medullated fibres is not materially altered by its presence. The refractive external border of the medullary sheath entirely prevents the extremely thin feebly refracting sheath of Schwann from being seen. But the resistance and firmness of the several nerve fibres are extraordinarily augmented by it, and the facility with which long portions of the fibres may be isolated in the peripheric nerves depends essentially on its presence. It prevents also the occurrence of the phenomena due to imbibition of fluids by the medullary portion of the nerves, as well as the formation of varicosities which are so characteristic of the medullated fibres of the nervous centres (fig. 19). The extraordinary differences in appearance and consistence exhibited by fibres of equal size, and similarly composed of axis cylinder and medullary sheath, but belonging respectively to the central and peripheric portions of the nervous system, are essentially referrible to the

presence or absence of this sheath of Schwann. In some instances the sheath is sufficiently thick to admit of measurement, as, for example, in the solitary nerve fibres that run in the mesentery of the frog; or in the electrical organs of the torpedo, where it attains a still greater thickness;* or it may even consist of a series of interlacing tubes, as in the nerves supplying the electrical organ of the electrical eel (Malapterurus), which are as thick as a knitting-needle, and still contain only a single medullated primitive nerve fibre.† In these instances the nuclei in the sheath are also much more distinct. If the sheath be very thin, it only becomes visible in the fresh state projecting for a short distance beyond the torn extremity of the fibres. Destruction and removal of the nerve medulla, in consequence of putrefaction or the action of reagents (concentrated acids, alcohol, and ether, which last dissolves the fat of the medullary sheath), are in such cases the only means by which the sheath of Schwann can be more distinctly demonstrated.

Just as a delicate sheath of Schwann, investing the medullary portion of the nerve, is scarcely perceptible in the fresh state of the nerve, so is it with great difficulty that an axis cylinder can be distinguished within the fresh medullary sheath. The bright lines which limit externally the highly refractive substance of the latter material, and the scroll-like contour lines which are occasioned by the gradually progressing coagulation of the nerve medulla, usually prevent the difference in the refractive power between the axis cylinder and the medulla from being observed. On the other hand it is easy to isolate the axis cylinder, at all events for short distances, in the medullated fibres of the central organs, when the sheath of Schwann is deficient; and it may thus be demonstrated from an examination of perfectly fresh specimens that in thick medullated fibres it is thick; in thin fibres, thin; appearing in the form of a pale fibre with the peculiarities above described. Moreover, it is possible in the perfectly fresh thick medullated fibres of the central organs

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* See Rud. Wagner, *Uber d. fein. Bau der Elect. Organes im Zitterrochen*, 1847, fig. 3, *b*, and woodcut 23 in this work.

† Bilharz, *Das Elekt. Organ des Zitterwelses*, p. 21.

to recognise distinctly the axis cylinder, with its fibrillar and finely granular structure, *within the medullary sheath,* as is shown in fig. 21, taken from a fibre from a brain of the torpedo. On this ground I regard the last possible doubt concerning the formerly frequently contested pre-existence of the axis cylinder as entirely set aside.

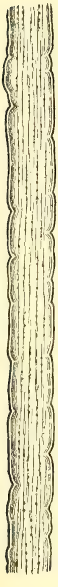

Fig. 21.

Broad medullated nerve fibre, taken fresh from the brain of the Torpedo, in the interior of which the structure of the axis cylinder can be recognised.

The isolation of the axis cylinder is remarkably facilitated by the previous application of fluids which gradually harden albuminous substances, such as dilute solutions of chromic acid, bichromate of potash, corrosive sublimate, and others. If these are allowed to act when in a moderate state of concentration, they harden the axis cylinder without any considerable troubling or granular coagulation, whilst the medullary sheath becomes crumbled and friable. In specimens of such medullated nerve fibres, as, for example, in those from the columns of the spinal cord, the axis cylinders may be either partially or completely isolated from the medullated sheath, for long tracts, with extreme ease; whilst the peripheric nerves, on account of the resistant sheath of Schwann, furnish preparations of less excellence. In order to see the axis cylinder *in situ*, fine transverse sections should be made through a carefully hardened spinal cord or nerve, and this should then be tinted in the ordinary method with carmine. The axis cylinder will now be found to be stained red, whilst the medullary sheath remains uncoloured. The unavoidable shrinking of the soft watery axis cylinder, which occurs when the preparation has been kept in alcohol, causes transverse sections of the reddened axis cylinder to present for the most part a dentated contour line, and to occupy much less space than might be expected from examination made upon fresh nerve fibres. Moreover, in tinted preparations, the red axis cylinder may be seen to run longitudinally in the unstained medullary sheath, especially if this be rendered transparent by treatment with creosote or oil

of turpentine. Transverse sections of the spinal cord are admirably adapted to exhibit the extraordinary variations that occur in the thickness of the axis cylinder, and the methods of Pflüger and Waldeyer are those which are best adapted to bring the axis cylinder speedily into view in fresh nerves. Pflüger's plan consists in adding a drop of collodion, Waldeyer's in adding a drop of chloroform, to the preparation, in as dry a state as possible, and covering with a thin glass. The medullary sheath will then be found to have lost its brilliancy, and in the greater number of nerve fibres the axis cylinder appears very distinctly as a finely granular central fibre.

We are in possession of extended observations by Bidder and Volkmann,* in reference to the difference in thickness existing amongst the peripheric medullated fibres, and especially between the cerebro-spinal and sympathetic fibres, which is very considerable.

A fourth form of nerve fibre may be added to those already described, which also occurs in the peripheric nerves, but is distinguished from the foregoing by the absence of the medullary sheath, and is on this account usually described as the peripheric non-medullated nerve fibre. These consist of fibres composed of a thicker or thinner bundle of primitive nerve fibrils, according to the kind of axis cylinder present, united together by a nucleated sheath of Schwann. All the branches of the olfactory nerve in the mucous membrane of the nose of all Vertebrates consist of such non-medullated nerve fibres. They are also of frequent occurrence in the sympathetic, the branches of which, distributed to the intestines, are often entirely composed of them ; as, for example, the thick splenic nerves of Ruminants, which are often more than a millimeter in diameter. It was here that Remak first observed them,† and hence the non-medullated sympathetic fibres bear the name of Remak's fibres. Remak himself subsequently called them ganglionic fibres.‡ Some fibres show the fibrillar structure much more distinctly than others, as was

* *Die Selbstandigkeit des Sympathischen Nervensystems.* Leipzig, 1842.

† *Observationes Anatomicæ et Microscopicæ de Systematis Nervosi Structura.* Berol., 1838.

‡ *Monatsberichte der Berliner Akademie*, 1853, 12th May.

remarked by Pflüger,* in the course of his investigations on the nerves of the salivary glands, on which account he divided them into two varieties. It is this kind of nerve fibre which, with few exceptions, is present amongst the Invertebrata. Nerve cords, which consist of such fibres, do not possess the bright

Fig. 22.

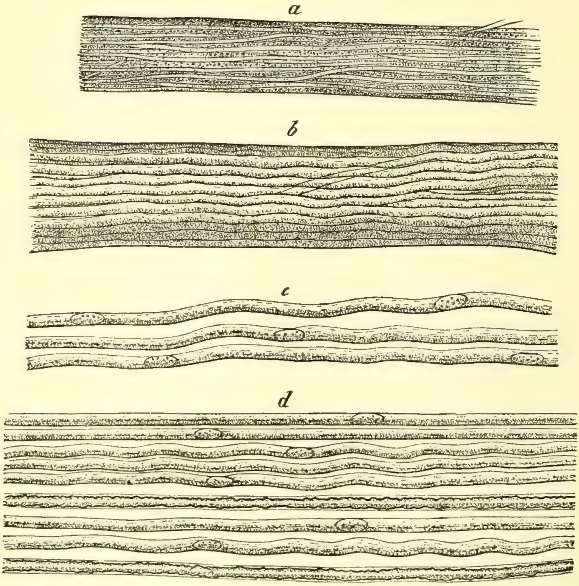

Fig. 22. Medullated nerve fibres. *a*, from the olfactory nerve of the Pike; *b*, from the olfactory nerve of Man; *c*, from the sympathetic (splenic nerve) of the Ox; *d*, from the nerve passing to the organ of Jacobson in the Sheep. In this specimen are two medullated fibres.

glancing appearance of ordinary nerves, but are semi-transparent grey, gelatinous, and resemble embryonic tendinous tissue. If they are freed from the denser connective tissue which invests them, they can be broken up into their constituent fibres as easily as other nerves, which is a consequence

* *Die Endigungen der Absonderungsnerven in den Speicheldrusen,* "On the Mode of Termination of the Secretory Nerves in the Salivary Glands." Bonn., 1866, p. 31.

of the firm consistence of the sheath of Schwann surrounding each fibre. The diameter of these non-medullated nerve fibres varies very considerably. In the sympathetic they scarcely exceed that of the medium-sized medullated fibres, but in the olfactory nerves of many animals fibres may be found at least three or four times thicker than the largest medullated fibres. Such thick fibres are shown in fig. 22, *a*, taken from the nasal fossa of a pike, consisting, when fresh, of a very soft, almost fluid, finely granular mass, with parallel striæ, contained in a transparent and structureless sharply defined sheath, in which, on the addition of acetic acid, nuclei make their appearance. By carefully hardening the specimen the fibrillar structure becomes very distinct, whilst at the same time the whole contents of the sheath may be broken up into fibrillæ of the nature of primitive nerve fibrils, between which the fine granules and molecules are interspersed to constitute an interfibrillar mass. In Man and most other vertebrate animals the fibres of the olfactory nerve are of less diameter than in fish, and resemble rather those of the sympathetic nerve, except that they are arranged in bundles within a common nucleated sheath, so that funiculi are formed similar to those shown in the subjoined fig. *b*, taken from man. Here, as in the sympathetic nerve *c*, the substance of the individual fibres is fibrillar, and finely punctated, and probably consists of primitive fibrillæ and an interfibrillar substance.

According to the preceding account of the structure of the nerve fibres, the following kinds may be distinguished:—

1. Primitive fibrils.
2. Fasciculi of primitive fibrils.
3. Primitive fibrils with medullary sheath.
4. Fasciculi of primitive fibrils with medullary sheath.
5. Fasciculi of primitive fibrils, invested by the sheath of Schwann (as in the non-medullated nerve fibres of the sympathetic, the olfactory nerve, and the nerves of the greater number of invertebrate animals).
6. Fasciculi of primitive fibrils, with medullary sheath and the sheath of Schwann (as the fibres of most of the cerebro-spinal nerves).

1 and 2 may be distinguished as *naked* axis cylinders; and

where they are invested by a sheath, as simply axis cylinders. It remains undecided whether nerve fibres exist, possessing a medullary sheath and the sheath of Schwann, the axis cylinder of which is formed by a single primitive nerve fibril.

If the nerve fibres be divided into two groups, according to the presence or absence of the medullary sheath, they may be further subdivided into

I. Non-medullated fibres.
   1. Primitive fibrils.
   2. Fasciculi of primitive fibrils.
   3. These last, with a sheath of Schwann.

II. Medullated fibres.
   1. Primitive fibrils with medullary sheath.
   2. Fasciculi of primitive fibrils with medullary sheath.
   3. These last with a sheath of Schwann.

We see then that the primitive fibril forms the elementary constituent of all nerve fibres. The variations that are observed are dependent on the number of the fibrils united together to form one cord, and upon the absence or presence of the medullary sheath and the sheath of Schwann. It is at once obvious how complicated a structure one of the so-called medullated primitive nerve fibres is when it is found to be composed of a bundle of primitive fibrils united by interfibrillar material constituting the axis cylinder, and of two investing sheaths.

The foregoing description differs from that generally received in the acceptance of the primitive fibrils, as the ultimate structural elements of the nerve fibres. I have already elsewhere* shown the probability of the existence of a fibrillar structure in the non-medullated fibres of the olfactory and sympathetic nerves, which the greater number of observers have regarded as purely granular rather than fibrous ; and my views have been supported by later observers, as Waldeyer,† Pflüger,‡ and others. We must here also take into consideration the similarity of the nerve fibres of the greater number of

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* *Untersuchungen über den Bau der Nasenschleimhaut*, p. 63.

† *Zeitschrift für rationelle Medicin*, Band xx., 1863, p. 202.

‡ *Die Endigungen der Absonderungsnerven in die Speicheldrüsen*, 1866, p. 31.

invertebrate animals, which all recent observers agree in describing as consisting of fasciculi of fibrils with interfibrillar granular substance.* Many Crustacea make exceptions to this, but only in so far that in them a structure analogous to the medullary sheath is present, in the interior of which fasciculi of fibrils lie enclosed, forming a kind of axis cylinder.†

Since their first discovery by Remak, the axis cylinders of the medullated nerve fibres of man and other vertebrates have repeatedly been held to exhibit a fibrillar structure. Remak himself described the axis cylinder, or as he termed it, believing it to be hollow, the axis tube, as marked by parallel lines, and regarded this as an indication of its fibrous nature.‡ His followers, however, became more and more convinced that the axis cylinder was a homogeneous structure, and this has recently been maintained by Waldeyer, to whom we are indebted for a laborious work on the subject.§ Waldeyer admits the probability of the origin of the axis cylinder from isolated fibrils in the nerve centres, just as he acknowledges that it splits peripherically into fibrils, but he holds that in its course it is a homogeneous structure.

Kölliker has arrived at the same result, since after adducing numerous arguments in favour of the fibrillar nature of the axis cylinder, he concludes with these words: "There is no absolute and decisive proof of fibrillation in the axis cylinder."‖

I am very far from denying that the axis cylinder, as it is ordinarily brought into view, gives the impression rather of a homogeneous than of a fibrillated cord. There is no doubt that when examined with moderate powers, and when hardened by the ordinary methods, its substance does appear homogeneous, or presents only a linear arrangement of fine molecules. But in proportion as the process of hardening is avoided in the prosecution of the investigation, and the structures are maintained, both as regards their consistence and refractive powers, in a state analogous to the fresh condition, especially when high magnifying powers are employed, so much the more clearly am I able to recognise a parallel striation and a substance of a finely granular nature between the striæ, which are appearances that I can only refer to the axis cylinder being constructed of fibrils, and

* Cf. especially Leydig, *Lehrbuch der Histologie des Menschen und der Thiere*, 1857.

† Remak and Häckel, the last in Müller's *Archiv*, 1857, p. 469.

‡ *Observationes Anatomicæ*, etc., 1838, p. 2, note 2.

§ *Zeitschrift für rationelle Medicin*, Band xx., 1863, p. 193.

‖ *Gewebelehre*, fifth Aufl., 1867, p. 244.

an interfibrillar substance. For this investigation I especially employ the lateral columns of the spinal cord with their thick medullated fibres, from which, on account of the absence of the sheath of Schwann, it is easy to isolate the axis cylinder, not only when quite fresh, with the addition only of a little serum, but still better after twenty-four hours' or more maceration in solution of iodine in serum, in which the axis cylinder becomes slightly hardened without shrinking or otherwise materially altering in appearance. Perosmic acid is also here of great service, solutions of which, varying in strength from one-half to one-eighth per cent., acting for a short time on the axis cylinder, harden it without materially changing its volume, and without producing a trace of granular coagulation. Axis cylinders thus freed from the medullary sheath show with remarkable distinctness the characters of parallel striation. But even whilst still contained within the medullary sheath, the fibrous and granular structure of the axis cylinder may be observed, as I was first convinced from observations made on the thick fibres of the brain of the torpedo, which possesses a proportionately thin medullary sheath.*

A decisive argument in favour of the fibrillar structure of the axis cylinder is derived from the observation of its origin from the great nerve cells of the spinal cord or of the brain. In regard to this point I must refer to the following account, and to the essay I have just cited, in which the particular observations are given, and will only mention here that the fibrils which emerge in a convergent direction from the cell substance, in order to form the axis cylinder process of the cells, unite, and are often far removed from one another by interfibrillar material (see figs. 18, 29, and 30, at *a*.) The formation of the proper axis cylinder results from a diminution in the quantity of the interfibrillar material, whilst the fibrils become more closely approximated in their parallel course, so that ultimately only a very small quantity of interfibrillar substance remains. In the periphery also it is not difficult to see the fibrillar character of solitary axis cylinders, as, for example, in the corpuscles of Vater and Pacini, as was shown to me by Dr. Grandry, providing the specimens are examined in the perfectly fresh state, without other addition than that of serum, and with sufficiently high powers.

I consider it, indeed, to be possible that, notwithstanding these

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* See my Essay, entitled *Observationes de cellularum, fibrarumque nervearum Structura, Bonner Universitäts Programm*, 1868, fig. 5, and the preceding woodcut, 21, p. 154.

observations, axis cylinders exist in which the original fibrillar nature is entirely lost by fusion of the fibrils with each other, and which have thus become homogeneous ; but I regard the principle as correct, that the thicker axis cylinders are composed of several primitive fibrils, since these converge at the centric, and for the most part separate from one another at the peripheric extremity. On physiological grounds also I maintain the possibility of isolated conduction in these constituent fibrils, even when no trace of interfibrillar substance is present.

I may just add that my views on these points differ essentially from those of Stilling,* who indeed regards the axis cylinder as a complicated fibrous structure, but distributes his elementary fibrils generally on the surface, and considers that they unite with constituents of the nerve and medulla, which also again consists, according to him, of fine fibres or tubules. Stilling, as is well known, has not been able to distinguish the preformed structure from the products of coagulation that occur in nerve fibres hardened in chromic acid.

Both naked axis cylinders, and those enclosed in a medullary sheath, offer some remarkable and unexplained peculiarities when they are saturated with dilute solutions of nitrate of silver in the dark, and are then exposed to light. After Frommann,† who made the first observations on the point, the best subsequent investigations have been made by Dr. Grandry.‡ As a result of this treatment there occurs in the axis cylinder a fine transverse striation, caused by the partial deposition of brownish-black silver compounds, which is here and there so regular as to remind the observer of the structure of striated muscular tissue, though in other parts it exhibits great irregularity. When the action of light has been more protracted, the appearance in question gradually disappears, and the whole becomes equably tinted of a brownish black. As Grandry remarks, however, not only the axis cylinder, but also the branched processes of the ganglion cells, and frequently the cells themselves, exhibit this striation in a very surprising manner. No one has hitherto succeeded in showing any relation between these appearances and the finer structure of the parts.

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* *Neue Untersuchungen über den Bau des Rückenmarkes*, 1859, p. 708.

† Virchow's *Archiv*, Band xxxi., Taf. 6, figs. 11 to 16.

‡ *Recherches sur la Structure intime du cylindre de l'axe et des cellules nerveuses*, *Bulletin de l'Academie Royale du Belgique*, *Mars*, 1868.

1. Division of the Nerve Fibres.

A peculiar feature presented by the nerve fibres in their course is their division. This frequently occurs near their peripheric extremity, but is also to be observed in the nerve centres, and occasionally in the nerve trunks. It may take place in all kinds of nerve fibres, with the exception of the primitive fibrils. Branched and ramified fasciculi of primitive fibrils are composed of the processes of many multipolar ganglion cells. In the olfactory nerve may be seen the repeated subdivisions, quickly following each other, of non-medullated fibres provided with a sheath of Schwann, with the sheath prolonged upon the branches.* The mode of division, however, that has been most frequently described is that of the medullated fibres, such as is seen, for example, in the nerves distributed to muscle.† This mode of division is usually dichotomous, and affects all the constituents of the nerve fibre. The division of the fibrillar axis cylinder probably consists only in a gradual process of isolation of the associated primitive fibrils. The medullary sheath is continued at the point of division over the branches, and is finally lost at their extremities. It is very remarkable that at the point of division, in consequence of a sudden diminution in the quantity of the nerve medulla, an attenuation of the nerve fibre occurs, whilst beyond this point, when the division is completed, the medulla is again found in its ordinary proportion. The sheath of Schwann divides in precisely the same manner. As the branches after division are much thicker when taken collectively than the trunk from which they proceed,

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* This may be particularly well observed in the thin plates of the nasal fossæ of rays and of sharks. Max Schultze, *Bau der Nasenschleinhaut*, Taf. 4, fig. 8, v. 9.

† See in particular Reichert and Müller's *Archiv*, 1851, p. 29. E. Brücke and Joh. Müller were the first who observed the divisions of medullated nerve fibres in muscle. See the last mentioned author's *Handbuch der Physiologie*, fourth edition, Band i., p. 524. Paul Savi was the first who saw the primary divisions of medullated nerve fibres in the electric organs of the Torpedo, in 1844.

whilst the axis cylinders diminish, it is obvious that the sheaths must augment in thickness. This holds in particular for the medullary sheath, the thickness of which is proportionately

Fig. 23.

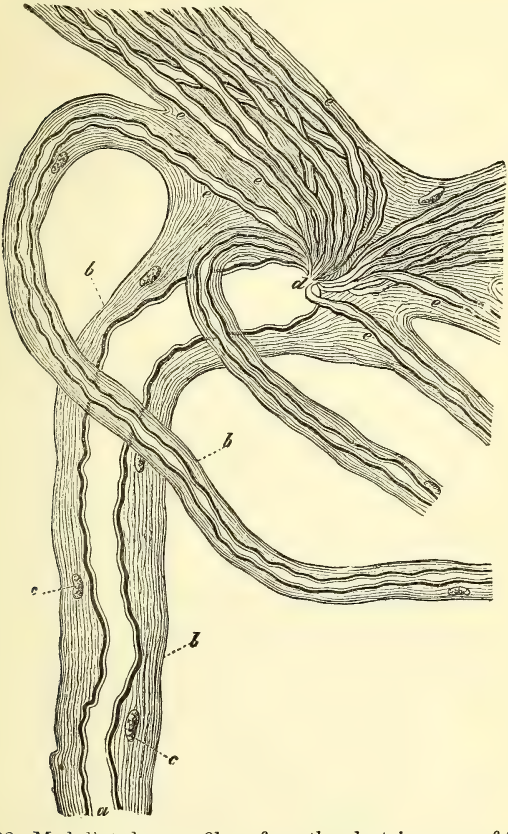

Fig. 23. Medullated nerve fibre, from the electric organ of the Torpedo, at the point of division, presenting a very thick sheath of Schwann. *a*, trunk fibre ; *b*, sheath ; *c*, nucleus of the sheath ; *d*, point of division ; *e*, branches. After R. Wagner.

much greater when the axis cylinder is thin than when it is thick. Instead of the dichotomous division, three, four, or more, even up to five and twenty branches may suddenly arise

from a single trunk fibre, as was first observed by Rud. Wagner in the nerves of the electric organ of the Torpedo.* By far the most remarkable example of nerve division occurs, however, in the electric eel (Malapterurus electricus). Here, according to Bilharz, each of the two electric organs which lie like masses of bacon-fat beneath the skin, receives a nerve from the medulla oblongata, consisting of only a single medullated fibre, having a diameter of 0·025 millimeters,† which, in order that it may give a peripheric terminal fibre to each electrical plate, must divide millions of times.

The sheath of Schwann disappears sooner or later in the process of division, and is consequently absent in the ultimate fibrils, as may be seen, for example, in the nerves of the cornea. Here the medulla also sooner or later disappears from the surface of the axis cylinder. Coincidently, or somewhat later, the sheath of Schwann can no longer be distinguished, the axis cylinder, which alone remains, repeatedly divides, and the fine primitive fibrillæ, as first demonstrated by Hoyer‡ and Cohnheim,§ ultimately project from the sub-epithelial tissue between the cells of the tesselated epithelial layer of the conjunctiva corneæ, and terminate by free extremities at the surface. The same appearance may be seen in many other nerves, as in the acoustic and optic, in the nerves of the tongue, in those distributed to the glands and elsewhere, though in these instances each primitive fibril is connected with a peculiar terminal apparatus, which will be hereafter described. In many parts, however, the division into primitive fibrils does not take place; that is to say, an axis cylinder of appreciable diameter terminates, so far as we at present know, without previously breaking up into the finest nerve filaments. The above-mentioned examples, the nerves distributed to many electrical organs, to the transversely striated muscles, the Vater's (Pacini's) cor-

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* *Feiner Bau der Elekt. Organes im Zitterrochen,* "Minute Anatomy of the Electric Organs of the Torpedo," 1847, p. 17.

† According to Bilharz, *loc. cit.*, p. 22—¹90iii.

‡ *Uber die Endigungen der sensibeln Nerven in der Hornhaut,* Virchow's *Archiv*, Band xxxviii., 1867, p. 343.

§ Reichert and Du Bois Reymonds' *Archiv*, 1866, p. 180.

puscles, exhibit, in part at least, when carefully examined, no exception to this rule.

2. Of the Peripheric Terminal Organs.

The peripheric division into primitive fibrils appears to occur in all the nerves of special sense, but especially in those cases where perception of a great variety of impressions occurs within a very limited space. Peculiar terminal organs are found in such instances in connection with each fibre, of which a more detailed description will be given in the consideration of the different senses, but which will be here only regarded from a general point of view. In the nasal mucous membrane, fusiform easily alterable cells are found occupying interspaces between the pallisade-like cells of the olfactory region. These possess a centric and a peripheric process, of which the former exactly resembles the primitive nerve fibrils of the olfactory nerves,* whilst the latter either ends at the level of the free surface of the epithelial cells, as in man, mammals, and fishes, or extends beyond this surface in the form of a long stiff hair, or of several finer hairs, analogous to cilia, but incapable of movement.

I have named these cells *olfactory cells*, and the hairs *olfactory hairs*. The general relations are the same in the mucous membrane of the tongue as Axel Key† has shown in the papillæ fungiformes of the frog, and Schwalbe‡ and Loven§ in the gustatory cells of the papillæ circumvallatæ, and of some of the fungiformes in man and mammals. These terminal organs corresponding to the olfactory cells may be termed *gustatory*

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* The existence of these cells was first recognised by Eckhard in the frog. See his *Beiträge zur Anatomie u. Physiologie*, Band i., 1855, p. 17, Taf. 5, figs. 3, 4 *c*; and a discussion on their relation to the Nervous System will be found in Schultze's Essay in the *Monatsberichte der Berliner Akademie*, 1856, November, p. 504, and at still greater length in Max Schultze's *Untersuchungen über den Bau der Nasenschleimhaut*, Halle, 1862, with five plates.

† Müller's *Archiv*, 1861, p. 329.

‡ *Archiv für Mikroskop. Anatomie*, Band iii., p. 154; Band iv., p. 154.

§ *Idem*, Band iv., p. 96.

cells. Similar conditions are found in the auditory organs, since in those parts where the nerve terminations are simple, the terminal branches of the medullated acoustic fibres, after losing their medullary sheath, penetrate between the epithelial cells, especially between those of the otolith sacs and of the ampullæ of the semi-circular canals, and after breaking up into primitive fibrils become continuous with peculiar ciliated auditory cells.* The mode of termination of the nerves in the cochlea is of greater complexity, especially because a portion of the non-nervous cells of the epithelial investment of the cochlear canal develops into the several structures forming the organ of Corti. But even here the terminal nerve structures appear to consist of cells supporting hairs, which are continuous with extraordinarily delicate non-medullated nerve filaments (primitive fibrils). The terminal nerve apparatus of the optic nerve in the retina presents quite peculiar features. Here are found the *layer of rods and cones,* and the nucleated external granules, which last, like the terminal apparatus of the olfactory nerve, appear as fusiform cells, with a centric and a peripheric process. The centric process of the rods is a single primitive fibril, but that of the cones is a fasciculus of primitive fibrils.† The peripheric process terminates in the case of the so-called rods and cones in an essentially similar manner, the extremity in each consisting of a pale inner segment resembling ganglionic cell substance, and a bright highly refractile external segment, which is separated from the former by a sharply defined line, and which in the

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* See Max Schultze's *Ueber die Endigungsweise des Hörnerven im Labyrinth,* Müller's *Archiv,* 1858, p. 343; Franz Eilh. Schulze in *idem,* 1862, p. 381; Odenius, *Archiv für Mikroskopische Anatomie,* Band iii., p. 115. Hasse so far gives a different account, in that he has not been able to observe the division of the axis cylinder into finer filaments (primitive fibrils). See others in *Zeits. für wissens. Zool.,* Bd. xvii., p. 638; Bd. xviii., p. 89. I must, however, maintain the correctness of my assertions respecting and illustrations of the above-described objects. The consideration of the auditory organ of invertebrate animals is of great importance in regard to the relations in question. See Hensen, *Zeitschrift für wissenschaftliche Zoologie,* Band xiii., p. 319, "On the Auditory Organs of the Crab."

† Max Schultze, *Archiv für Mikroskopische Anatomie,* Band ii., Taf. 10.

rods is of cylindrical, and in the cones of conical form. The structure of the outer segments, which, in all probability, constitute the proper terminal structures, upon the excitation of which perception depends, differs from that of any other nervous organ, especially in its consisting of a series of thin plates superimposed on one another in the direction of its long axis.* The tactile nerves of the skin, lastly, terminate in the so-called *tactile corpuscles,* which are oval or spherical, very soft, and easily alterable bodies, occupying the interior of many tactile papillæ of the skin,† each of which is continuous with one or more medullated nerve fibres that divide in their interior, though up to the present time the precise mode of termination of the primitive fibrils in them has not been completely elucidated.

In immediate relation to the sense of touch stand also in all probability the nerve hairs found on the surface of young fish and naked amphibia, which have been ascribed by F. E. Schulze,‡ and the arrangement of which in the form of pencils or brushes calls to mind the nerve hairs in the ampullæ of the auditory organ. These appear to be well adapted for the perception of movements of the water in which the animals live. In fishes also is found the lateral canal system, with the nerve bulbs described by Leydig. I have also observed a very similar disposition of the nerves in regard to hair-bearing epithelial cells in the vesicles of Savi present in the torpedo.§ According to recent investigations by Franz Boll, the highly nervous ampullæ of the so-called mucous canals of the head of rays and sharks are covered with cell-supporting hairs.

We may also regard the *corpuscles of Vater or Pacini* as

* Max Schultze, *Archiv für Mikroskopische Anatomie,* Band iii., p. 215. A reference may also be made to the differentiation of one or several axial fibres in the outer segment, first observed by Ritter. See especially Hensen, Virchow's *Archiv,* Band xxxix., p. 475, Taf. 12.

† We owe the discovery of these structures to Meissner and Rud. Wagner. See Göttinger, *Nachrichten,* 1852, No. 2; or in more detail Meissner, *Beiträge zur Anatomie und Physiologie der Haut.* Leipzig, 1853.

‡ Müller's *Archiv,* 1861, p. 759.

§ *Untersuchungen über den Bau der Nasenschleimhaut,* 1862, p. 11. In this essay will be found a more detailed account of the relations at present known to exist between nerves and epithelial investments.

constituting terminal organs of the sensory nerves. These are most commonly found in man in the subcutaneous connective tissue of the sides of the fingers and toes, seated on the volar and plantar nerves; also on the nerves supplying joints, and in the nerves coursing between various muscles of the trunk and extremities;* in animals, however, they are found in many other parts of the body, and may be most easily obtained for examination from the mesentery of the cat. Each of these corpuscles receives a medullated nerve fibre, which does not again emerge from it. The corpuscle itself consists of many concentrically arranged layers of connective tissue, becoming always more closely packed near the centre, and surrounding a cavity filled with soft abundantly nucleated and very easily alterable material, which undergoes coagulation after death, and into the interior of which the nerve fibres penetrate. These, after they have lost the medullary sheath and the sheath of Schwann, which becomes continuous with the laminated sheaths of connective tissue investing the corpuscle, consist only of the axis cylinder, which terminates in a little bulb.† Dr. Grandry, who has examined the Pacinian corpuscles with higher magnifying powers than appear to have been previously employed, observed a very distinct fibrous structure in the axis cylinder in their interior, and also that the terminal bulbs consist of finely granular substance, from which the diverging terminal fibrils may be clearly distinguished. Closely allied to the foregoing are the numerous terminal nerve corpuscles described and depicted by Krause as existing in the conjunctiva, the genitals, and other parts of the body, which differ from the Pacinian corpuscles only in the absence of a thick laminated investment.‡

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* See Rauber, *Untersuchungen über das Vorkommen und die Bedeutung der Vater'schen Körper*, "Researches on the Distribution and Function of the Corpuscles of Vater," 1867.

† See the numerous illustrations of these corpuscles and their minute microscopic anatomy in Henle and Kölliker's Essay, *Ueber die Pacini'schen Körper an den Nerven des Menschen und der Saügethiere*, Zurich, 1844, which was followed by the work of Herbst, entitled *Die Pacini'sche Körper und ihre Bedeutung*, Göttingen, 1848. There are numerous recent investigations on the point, amongst others, those of Leydig, Krause, Kölliker, and Rauber.

‡ See W. Krause, *Die terminalen Körperchen*, 1860; *Anatomische*

The mode of termination of the nerves in the transversely striated muscles has been the subject of numerous researches, and we now know through those of Kühne, Engelmann, and others that axis cylinders of moderate thickness penetrate the sarcolemma of the muscular fibres, and either branch out to form the so-called terminal nerve plate, or, as in the frog, break up into primitive fibrils in the interior of the contractile sub-

Fig. 24.

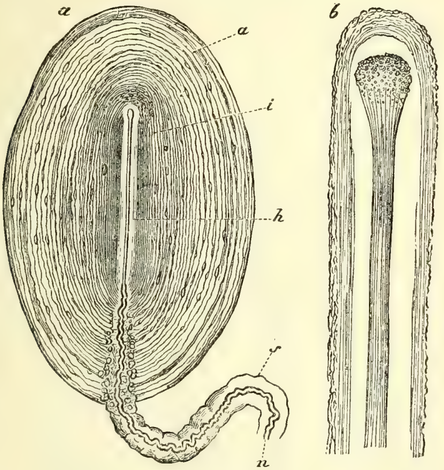

Fig. 24. *a*, Vater-Pacinian corpuscle from the mesentery of the Cat, examined with a low power—after E. Ecker; *b*, the end of the nerve fibre, consisting of a fibrillated axis cylinder, the fibrils of which are lost in a finely granular mass, magnified 1,000 linear—after Grandry.

stance, and therefore probably in the interfibrillar substance. Frankenhäusen has recently maintained that in the smooth muscular fibres there is a connection between the primitive nerve fibrils and the nucleoli of the fibre cells, on which point, however, the reader is referred, as in regard to the nerves of muscles generally, to the section on muscles.

A peculiar and remarkable mode of nerve termination is

Untersuchungen, 1861; Bense, *Die Nervenendigungen in der Geschlechts Organen, in der Zeitschrift für rationelle Medicin*, 1868, Band xxxiii., p. 1.

found in the electrical organs of those fish that are provided either with true or the so-called pseudo-electric organs (as the Torpedo, Malapterurus, and Gymnotus amongst the former, and the Raja and Mormyrus amongst the latter). The axis cylinders

Fig. 25.

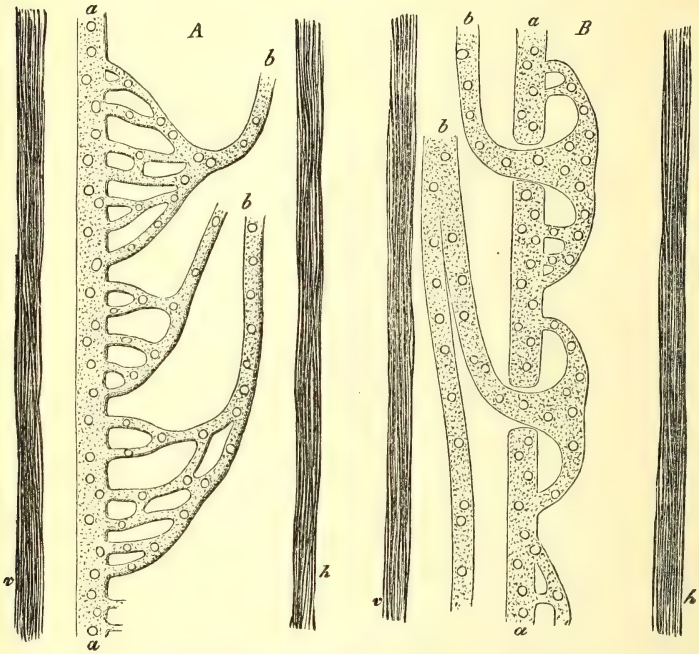

Fig. 25, A. From the electric organ of Mormyrus oxyrhyncus, and also as in the M. longipinnis and cyprinoides. *v* anterior, *h* posterior connective tissue septum; *a a*, electric plates; *b b*, nerves penetrating into their interior.

B. From the electric organ of Mormyrus dorsalis, and also as in the M. anguilloides. Lettering as in A.

of the nerve fibres, which pass to these organs from the nerve centres, here terminate in the so-called electrical plates, which are direct expansions of the nerve fibres in the form of remarkable discs, each of which lies in a small chamber of the organ formed by septa of connective tissue. Fig. 25, after Ecker

taken from the Mormyrus, shows the electrical plates forming direct expansions of the nerve-fibre substance, from which it appears that the nerve fibres penetrate foramina in the plates (as in some species of Mormyrus and Malapterurus) before they break up in its substance.

The point of entrance always occurs on one only of the two surfaces of the disk, and, indeed, on the same or corresponding surface of all the plates of the same animal; thus, for example, in the torpedo, in which the plates have a dorsal and ventral surface, the nerves are always applied to the ventral surface, the dorsal remaining smooth; consequently all these electric plates have a smooth free, and a rough surface to which the nerve fibres are attached, and these all look in the same direction. At the moment of the discharge in all the electric fishes hitherto examined, that side of the animal to which the rough surfaces of the electrical plates are turned is negative as compared with the opposite. In Malapterurus only a single primitive nerve fibre, which has just previously lost its medullary sheath, penetrates each plate; but in all other animals many fibres enter. The structure of these electric plates, composed of albuminous material, differs in two points from the former. The plates of the true electric organs are homogeneous disks, slightly uneven on their free surface, in the interior of which oval or spherical nuclei, surrounded here and there with a little finely granular substance, lie scattered at definite distances. The plates of the so-called pseudo-electric organs, on the other hand, exhibit similar nuclei, but their substance is not homogeneous, being marked by delicate, meandering, and looped systems of lines, which result from their complicated structure, composed of a number of layers of very thin curved plates. The tissue in some measure calls to mind that of the transversely striated muscles.*

* A. Ecker, *Untersuchungen zur Ichthyologie*, Freiburg, 1857; *Berichte der Naturf. Gesellschaft zu Freiburg*, 1858, No. 28. Max Schultze, *Uber Pseudo-electrik. Organ*, *Sitzungsberichte der Naturf. Gesellschaft in Halle*, 1857, p. 17; and in Müller's *Archiv*, 1858, p. 193. Also Bilharz, *Das Elektrik. Organ des Zitterwelses*, 1857; and Max Schultze, *Zur Kenntniss der Elektrik. Organ der Fische*, 2 Abtheilungen. Halle, 1858 and 1859.

In regard to the mode of termination of the nerves in glands, the investigations of Pflüger* on the salivary glands may here be mentioned, in which he showed that the extremities of the nerves formed such a connection with gland cells, that either the cells themselves or their nuclei constituted the terminal organ, as will be more explicitly described in the article on GLANDS.

Hensen has described the cutaneous nerves of the frog as terminating peripherically in the nucleoli of the cells of the epidermis.† They form extraordinarily fine fibres, which penetrate both the cells and nuclei, and in consequence of the frequent division of the nuclei are also themselves frequently bifurcated.

3. ON THE MODE OF ORIGIN OF THE NERVE FIBRES IN THE NERVE CENTRES.

The transition from the foregoing to the consideration of the central source or origin of the nerve fibres is to be found in the description of those nerve or ganglion cells which are intercalated in the course of the nerve fibres, and of the so-called ganglia. The microscopic examination of the ganglia of the brain and spinal cord, as well as of the sympathetic nerves, alike shows that the cells are to be regarded as an essential part of these structures, and that they exhibit a nucleus and nucleoli lying in a relatively considerable quantity of a dense finely granular and fibrillated cell substance, which is often tinged of a yellow colour. The greater number of these cells, when isolated in the perfectly fresh state in serum, are spheroidal; yet they are often also very irregular in outline, destitute of any doubly contoured investing membrane, and become broken up and disappear with the greatest facility. In sections made through fresh or hardened ganglia such cells appear to be arranged in layers surrounded by fibrous connective tissue, in which large numbers of both medullated and non-medullated nerve fibres

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* *Die Endigungen der Absonderungsnerven in die Speicheldrüsen.* Bonn., 1866.

† Virchow's *Archiv*, Band xxxi., p. 63, Taf. 2, fig. 14; *Archiv für Mikroskopische Anatomie*, Band iv., p. 121.

commonly lie imbedded. Each cell, however, occupies a kind of capsule composed of nucleated connective tissue, from the inner surface of which it retracts when acte l upon by strongly hardening fluids.

Fig. 26.

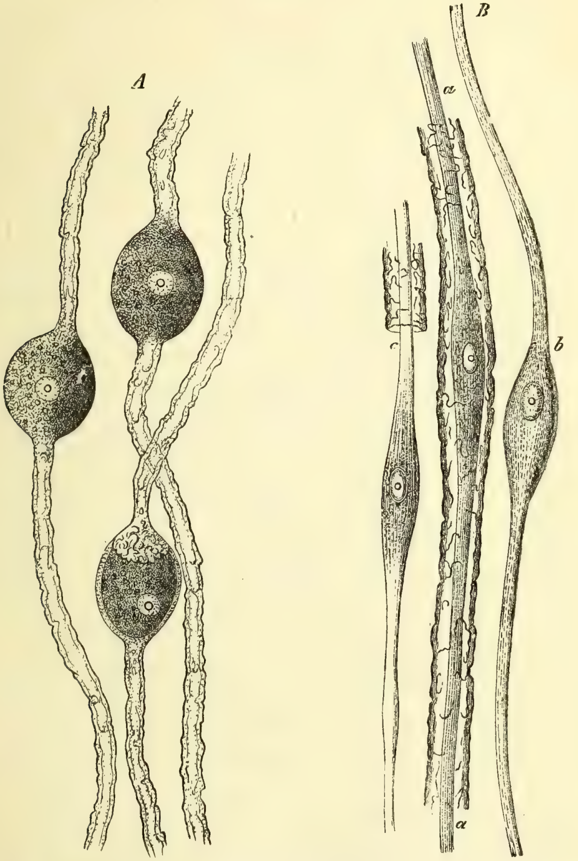

Fig. 26, A. Three bipolar ganglion cells, from the Ganglion Gasserii of the Pike—after Bidder.

B. Three bipolar ganglion cells, from the auditory nerve of the Pike. *a*, still contained in the medullary sheath; *b*, entirely; *c*, partially exposed, in order to show that these ganglion cells are only nucleated dilatations of the axis cylinder.

The majority, perhaps it may even be said all, of these cells possess processes, which, however, in the fresh state can be torn off with a facility proportionate to the difference in the consistence of the cell substance and the investing capsule of connective tissue. These processes are nerve fibres, as was first observed by Remak in the Vertebrata,* and by Helmholtz† amongst the Invertebrata. If only one be present, causing the cell to look like a berry attached to its stalk, it is termed unipolar; if there are two which are often connected with the opposite extremities of the cell, this is termed bipolar, and when there are several, it is multipolar. That these processes are nerve fibres is most clearly evident in certain bipolar ganglion cells, which are introduced in the course of those medullated nerve fibres that may easily be obtained from the perfectly fresh spinal ganglia of sharks and rays, where they were first noticed by Robin and Rudolph Wagner‡ in 1847; or from the Gasserian ganglion of the same animals, where I have been able to demonstrate their presence with great ease; or from the same ganglion of the osseous fishes (pike, according to Bidder); § or lastly, from the auditory nerve before its entrance into the sacculi of the labyrinth.|| The cell substance is here a continuation of the substance of the axis cylinder; it includes a nucleus and nucleoli; the medullary sheath usually ceases at the point of transition of the fibre into the nucleated enlargement of the axis cylinder, and reappears at the corresponding point on the opposite side; though it occasionally invests the entire cell, the cytoid enlargement of the axis cylinder in that case occasioning no interruption to the medullary sheath. It is obvious that such a ganglion cell is only a nucleated swelling of the axis cylinder. The fibrillated structure of the latter may be followed in the cell substance, although it is there in

* Froriep's *Notizen*, 1837, Nos. 47, 56, 58; *Observationes Anat. et Microscop. de Systematis Nervosi Structura*. Berol, 1838.

† *De fabrica Systematis Nervosi Evertebratorum, Diss. inaug.*, 1842.

‡ R. Wagner, *Neurologische Untersuchungen*, p. 7.

§ *Zur Lehre von dem Verhältniss der Ganglionkörper zu die Nervenfasern*, "On the relations of the Ganglia to the Nerve Fibres." Leipzig, 1847.

|| Max Schultze, *De Retinæ structura penitiori*. Bonn., 1859, fig. 7.

part concealed by the presence of a considerable quantity of the interfibrillar substance. And just as the medullary sheath is not essential to our conception of a nerve fibre, so we can only regard it as forming an accessory sheath to the ganglion cell, to which, indeed, it rarely constitutes a continuous investment. The sheath of Schwann, if present, is continued over the ganglion cell, and forms the above-mentioned capsule of nucleated connective tissue. It is, however, absent in the bipolar ganglion cells of the auditory nerve.

The structure of the spinal ganglia of other vertebrata and of man is more complex. It has been frequently observed, and has very recently been corroborated by the researches of Schwalbe,* that the cells of these ganglia each possesses for the most part only a single non-medullated process which runs towards the periphery, and which, according to Kölliker, subsequently becomes the axis cylinder of a medullated nerve fibre. Like the substance of the ganglion cells, it presents a fibrillated structure. From some of the cells, on the other hand, instead of a single process, several are given off, which, however, do not arise, as in fishes, from the opposite poles of the cells, and with the further course of which we are still unacquainted. Observations similar to these were made by Kölliker on the cells of the Gasserian ganglion.†

Like those of the spinal ganglia, the cells of the sympathetic ganglia are invested by dense connective tissue, and each possesses a proper nucleated capsule, proceeding from and continuous with the sheath of Schwann, covering the nerve fibres with which it is in connection. The number of these last here also varies to a considerable extent. In the sympathetic of the frog, which has been most frequently examined, there occur, besides such unipolar cells as have just been described, others from which two processes spring in close proximity, of which one winds spirally round the other. The minuter details respecting the mode of connection of these spiral fibres, which were first described by L. Beale‡ with the ganglion cells, is still

* *Archiv für Mikroskopische Anatomie*, Band iv., p. 45.

† *Handbuch der Gewebelehre*, 5. Auflage, p. 319.

‡ *Philosophical Transactions*, 1863, Vol. cliii., p. 539.

a subject of dispute, as is evident from the conflicting statements of J. Arnold,* Courvoisier,† Kölliker,‡ and others. The existence of multipolar cells in the large ganglia of the sympathetic, though contested by many, is certain, as I have myself found such cells both in children and in adults (fig. 27). Un-

Fig. 27.

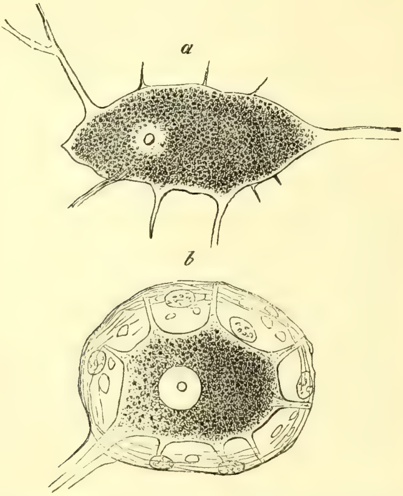

Fig. 27. Nerve cells from a lumbar sympathetic ganglion of an adult Man. *a*, without a sheath; *b*, with a sheath. The cell substance contains pigment of a vivid yellow tint, and is consequently darkly granular.

fortunately, on account of the surrounding fibrous connective tissue, it is impossible to isolate the processes for any considerable portion of their length.

The processes in connection with the ganglion cells of the spinal cord which furnish axis cylinders to the spinal nerves, those in the anterior horns of the grey matter proceeding to the motor, and those in the posterior horns to the sensory nerves, are much more accurately known. The researches of Deiters in particular have demonstrated that from every gan-

* Virchow's *Archiv*, Bände xxviii. and xxxii.
† *Archiv für Mikroskopische Anatomie*, Band ii., p. 13, and Band iii.
‡ *Handbuch der Gewebelehre*, 5. Auflage, p. 254.

Fig. 28.

Fig. 28. Multipolar ganglion cell, from the anterior horn of the grey substance of the spinal cord of the Ox—after **Deiters.**
a, axis cylinder process ; *b*, branched processes. Magnified 300 diameters.

glion cell, however numerous its processes may be, only one peripherically coursing axis cylinder arises. This runs without branching, obtains, sooner or later, a medullary sheath, and passes into one of the roots of the nerves. It possesses a fibrillar structure, as I have myself most distinctly seen, both in sensory and motor and ganglion cells. The other processes of these ganglion cells, the number of which is greater in the large cells of the anterior horns than in those of the posterior, branch in an arborescent manner very soon after their origin. Their structure is also distinctly fibrillar; but the quantity of interfibrillar granular substance they contain is greater than in the axis-cylinder process. The fine filaments (primitive fibrils), which result from their ramification, soon evade observation, and their ultimate destination is unknown. Deiters believes that in some few instances he has observed them to become invested with a delicate medullary sheath.

The fibrils of both kinds of processes arise from the ganglion cell substance itself, which exhibits a fibrillar structure throughout, though a finely granular substance, often containing yellowish or yellowish-brown pigment, also exists between the fibrils; this may extend into the branched processes, or after being interrupted for a greater or less extent, may again make its appearance in them. The fibrillar structure may be most distinctly perceived in the cortical portion of the ganglion cells, though it unquestionably extends into the interior. In many cases, and especially in young rather than in more fully developed ganglion cells, a considerable quantity of finely granular material appears to occupy the interior of the cell, and to surround the nucleus. The course of the fibrils within the ganglion cells is very complicated; they may be seen passing from the processes into the cell substance in a divergent manner in every direction, and are there lost in the confused whorl of decussating filaments. This structure exists in the perfectly fresh state, as may be seen in the large cells of the fresh spinal cord which have been isolated after the addition of serum, and is very distinct in preparations macerated in perosmic acid and other hardening agents, which either check the natural conversion of the fibrils after death into a granular mass, or which do not produce any granular coagulation.

Fig. 29.

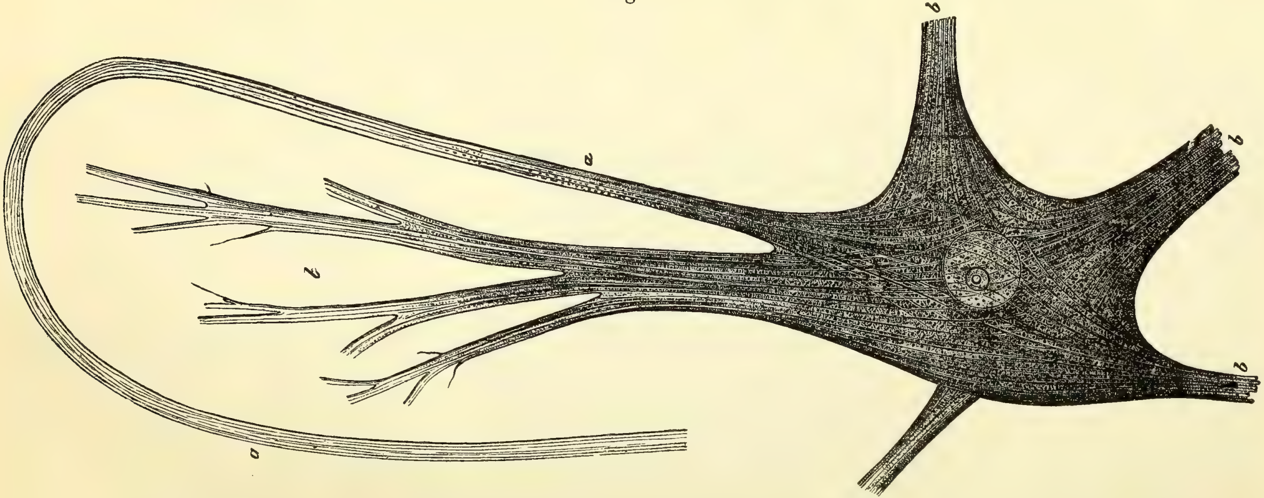

Fig. 29. A medium-sized ganglion cell from the anterior horn of the spinal cord of a Calf, isolated after short maceration in serum containing a little iodine in solution, x 600. Some of the processes are abruptly broken off, as may be seen in the three lower ones marked *b*; *a* is the axis-cylinder process.

Remak* first called attention to this fibrillar structure, and it was subsequently further investigated in the ganglion cells of various parts by Leydig, Beale, Frommann, Arnold, Kölliker, and myself,† although up to the present time there has not been complete agreement between the different observers in regard to its nature.

In consideration of the great difficulty experienced in isolating fresh ganglion cells, and in determining their distribution, it appeared to me worth while to subject to severe scrutiny, in the fresh state, those parts of the brain of the Torpedo in which, as has long been known, large ganglion cells, similar to the motor cells of the spinal cord, are accumulated in great numbers.‡

It was most convincingly shown here that the large cells removed from the living animal, and prepared in serum, in which they were capable of being easily isolated, possess, both in their processes and in their proper substance, an exquisitely delicate fibrillar structure. In large specimens the interfibrillar substance is strongly tinged of a yellow colour, and is in some parts coarsely granular. These circumstances render the investigation of the direction of the fibres difficult, so that young specimens are to be preferred for examination. Each of the numerous processes of these ganglion cells receives a compound fibril from the cell substance, giving the impression that the whole mass of fibrils given off by ganglion cells only traverse it. The nucleus of these cells is seen with a sharply defined outline lying imbedded in the finely granular fibrillated material, but does not appear to stand in any direct connection with the fibrils which cover its external surface. Its substance is homogeneous, and it contains in its interior a large nucleolus which stands out in strong relief as a highly refractive spherical body, and conceals one, or more rarely several, vacuolæ. We may regard such a ganglion cell, from which a peripherically directed nerve fibre proceeds, as representing the source

* *Monatsberichte der Akademie der Wissenschaften zu Berlin*, 1853.

† See Kölliker, *Handbuch der Gewebelehre*, 5. Auflage, p. 251, and the woodcut on p. 275.

‡ *Observationes de Structura cellularum fibrarumque nervearum. Bonner Universitäts Programm*, Aug., 1868.

Fig. 30.

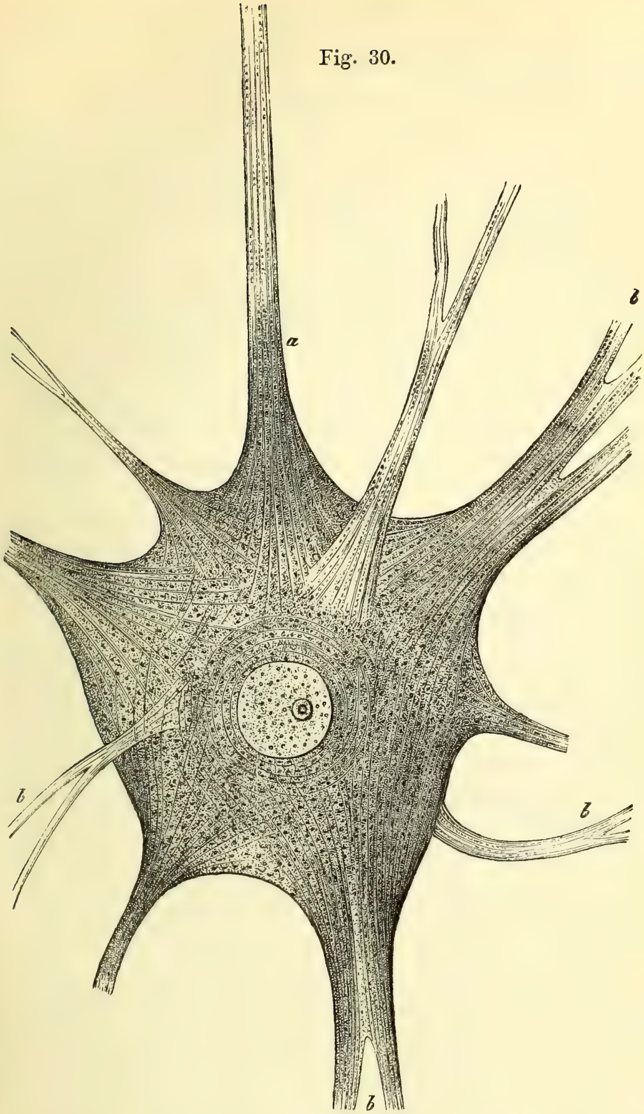

Fig. 30. Ganglion cells from the electric lobes of the brain of the Torpedo, medium-sized specimen, x 600. *a*, axis-cylinder process; the remainder, arborescent processes, recent. After short maceration in serum containing a little iodine.

and origin of this axis cylinder, but only in the sense that the fibrils which compose the axis cylinder are collected into a group from the arborescent processes of the cell; and thus the fibrils which are seen traversing the substance of the ganglion cell do not originate in the cell, but only undergo a kind of arrangement in it, and then pass to the axis-cylinder process, or extend into the other branched processes.

The researches of Deiters have rendered it probable that at the origins of the cerebral nerves the groups of ganglion cells which were described by Stilling under the term nerve nuclei, contain ganglion cells which closely resemble those of the anterior and posterior cornua of the spinal cord, especially in the circumstance that they give off only one peripherically directed axis-cylinder process, the remaining processes breaking up into a ramification of primitive fibrils.

It is well known that a considerable number of ganglion cells are found distributed through the brain, which do not directly give origin to peripherically coursing fibres; as, for example, the retort-shaped ganglion cells of the cortex of the cerebellum, and the peculiarly shaped cells of the grey cortical layer of the cerebrum, for the exact description of which we are indebted to the recent investigations of Rudolph Arndt* and Meynert.† In the former, according to Deiters,‡ the azygous process directed towards the white substance of the cerebellum corresponds to the axis-cylinder process; and it is known that the peripherically coursing processes of these cells branch in an arborescent manner. Other microscopists, as Gerlach,§ have observed ramifications occur in the centrically directed process. It is therefore scarcely justifiable, in the present state of our knowledge, to institute a precise comparison between these cells and those which are found in the spinal cord. On the other hand, I have myself seen a fibrillar structure in these ganglion cells of the cerebellum and their peripheric processes with the utmost distinctness, as, indeed, had previously been observed

* *Archiv für Mikroskopische Anatomie*, Band iii., p. 441.

† *Vierteljahrschrift für Psychiatrie*, Bände i. and ii.

‡ *Loc. cit.*, p. 72.

§ *Mikroskop. Studien*, p. 11.

by Kölliker in their processes,* so that in this respect there does not appear to be any difference between the two sets of cells. The same holds good for the cells of the grey cortex of the cerebrum. As Meynert and Arndt state, these possess a thicker peripheric process and a large number of branched processes, which are directed towards the white substance. The ganglion cells have a more or less conical form, the base of the cone being directed to the white substance, and sending forth a number of processes which quickly ramify, whilst the apex of the cone is continuous with a single, longer, thicker, and at first unbranched process. In accordance with the observations of Meynert, however, I have seen this process, which has been compared to the axis-cylinder process, divide, sooner or later, in a dichotomous manner, and undergo further subdivision in cells which had been completely isolated by maceration in iodized serum. I have witnessed a similar division in the pedunculated ganglion cells of the Pes huffocampi major, respecting which Deiters† was of opinion that the thicker process, constituting the stalk of the cell, was an axis-cylinder process. Nevertheless, I am unable to admit that either these cells or those of the grey cortex of the brain can, without further investigation, be classified with the multipolar cells of the spinal cord. Still it is quite true that the cells of the cerebrum, as I have already observed, possess an exquisite fibrillar structure, and rather appear as a point of junction and intersection for nerve fibrils that are already developed, than as a point of origin for those which have not hitherto been in existence.

In addition to the larger cells of the cerebrum which have just been mentioned, an enormous number of smaller cells are found in that organ, the nuclei of which are invested by only a small quantity of cell substance. It has been demonstrated that some of these give off processes, of which the ultimate destination is certainly not known, but which are, nevertheless, sufficient to characterise the cells as nerve cells, and to distinguish them from the connective tissue cells that are undoubtedly present in the spongy connective tissue of the central organs

* *Handbuch der Gewebelehre*, 5. Auflage, 1867, p. 243.

† *Loc. cit.*, p. 66.

of the nervous system. Amongst these small cells, some are multipolar, some bipolar, and some unipolar. They form thick layers in the cerebellum, and both Gerlach* and more recently Franz Schulze† have shown that their processes consist of immeasurably fine fibrils. If we therefore venture to inquire into the central origin of the primitive fibrils in the brain and spinal cord, which appear to exist already completely formed in the larger ganglion cells, we may suppose that it is from these extremely small and, in part at least, unipolar nerve cells, though it must be admitted that this is pure hypothesis. In the present state of our knowledge, however well we may be acquainted with the peripheric mode of termination of a great number of nerve fibrils, it cannot be said that the mode of central origin of any single fibril has hitherto been proved. We may, however, conclude from analogy that the central extremity is to be sought either in the cell substance of the nerve cells, or in the nucleus, or in the nucleolus. Observations have been made which render all these three modes of central termination of the nerve fibrils probable; but no perfectly satisfactory conclusion can be said to have been as yet attained on this point; and it is even conceivable, according to my observations, that there is no actual termination of the fibrils in the brain or spinal cord; in other words, that all fibrils originate at the periphery, and thus only traverse the ganglion cells.

The question of the relation of the nerve fibres to the ganglion cells appears, from what has been stated above, to be still an open one on certain points. If the view long ago entertained, especially by Valentin, that the nerve fibres only coil round the ganglion cells, and do not enter into more direct connection with them, is opposed by the brilliant investigations of Remak and Helmholtz, still the question of the centric mode of origin of the nerve fibres has not yet been thoroughly solved. It is obvious that the mere interruption of a nerve fibre in some part of its course by a bipolar ganglion cell, as was so beautifully described and delineated by Bidder in 1847, affords no information respecting its centric origin. Such a ganglion cell is to be regarded

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* *Mikroskop. Studien*, Taf. 2.

† *Ueber der feineren Bau der Rinde des kleinen Gehirns*, "On the Minute Anatomy of the Cortex of the Cerebellum." Rostock, 1863, fig. 11.

as composed essentially of only a nucleated enlargement of the axis cylinder. If we pass to a more central portion of the nervous system, we meet with the multipolar ganglion cells of the spinal cord, or of the medulla oblongata, from which, according to the important discovery of Deiters, the axis cylinder of the fibre in question proceeds as an undivided process. The numerous other processes of the cell connect it, and by its means the axis cylinder, with more distant regions of the central organs, and probably also of the periphery of the body, but clearly do not entitle us to regard the ganglion cell as the exclusive origin of the nerve fibre. If we compare the axis-cylinder process with the stem of a plant and its divisions, and the peripheric terminal organs with the branches, leaves, and flowers, the ganglion cell is equivalent to the root stock, and the branched processes to the subterranean root fibres. It is requisite to follow these out in order to arrive at the extremity opposite to the peripheric termination. In consequence of the evidence I have adduced of the exquisitely delicate fibrillar structure of the ganglion cell substance, and of all its processes, a path is opened by which we may investigate the true central terminations of the fibrils entering into the composition of the axis cylinder. Unfortunately, the individual fibrils within the substance of the cells escape all accurate observation.

The above comparison of the ganglion cells and their processes with the root stock, stem, and root fibres of a plant, is, after all, like most comparisons, only an imperfect one. The branched processes of a multipolar ganglion cell, such, for instance, as may be found in the anterior horn of the spinal cord, have certainly not all been satisfactorily ascertained to pass as primitive fibrils to the axis-cylinder process; but rather this receives only a single group, the remainder extending as branched processes in other directions. Thus the ganglion cell constitutes a common point of union of numerous separate fibrils proceeding from widely different regions of the nervous system; and whilst one of these associated bundles becomes the axis cylinder of a fibre, and after becoming invested by a medullary sheath, immediately runs peripherically, the others pass in unknown directions.

It remains to consider whether, admitting that a large number of the fibrils are already formed, and only traverse the ganglion cells, there may not be some which do actually originate in these. In regard to this point, the interfibrillar granular substance is first to be noticed, which is probably a residue of the embryonic protoplasm, by the agency of which the fibrils are differentiated; a substance which possibly remains in greater abundance in the immediate vicinity of the

nucleus, and there retains a power allied to that which it possessed when in the embryonic state. Yet, however probable it may appear that the several fibres arise in and from this substance, no observations have as yet been made which establish it with perfect certainty. Another mode of origin of new fibrils or thicker fibres from the ganglion cells has, on the contrary, been suggested by various observers. Since Harless* stated that the nuclei and the nucleoli of the large cells of the brain of the torpedo were the points of origin of the nerve fibres, the same view has been entertained by many others in regard to other ganglion cells, and especially for those of the sympathetic of the frog, as in the first instance by Axmann, Lieberkühn, and Wagner, and subsequently by Beale, Arnold, Frommann, Jolly, and Courvoisier. But it was noticed by Frommann and Arnold† as occurring also in the cells of the spinal cord and in those of the brain; and Meynert stated that the nuclei and the nucleoli were centres for fibres, the fineness and delicacy of which render them comparable to our primitive fibrils. I agree with Kölliker and others, however, in the statement that this, at least, is not the ordinary condition, and I have not been more successful than Kölliker in obtaining any positive evidence of such a mode of origin of the fibres in question.

Although anastomoses occur between adjoining ganglion cells, it is a matter of much difficulty to acquire any certain information respecting the constancy or frequency of their occurrence. As there are ganglion cells with two nuclei, like those, for example, that, according to Guye and Schwalbe, are constantly met with in the sympathetic, and occasionally in the brain of the rabbit, so we may refer one form of the anastomoses occurring between ganglion cells to the type of bi-nucleated cells; those, namely, in which a short thick bridge unites two nucleated corpuscles with one another. Such anastomoses have recently been described by Meynert, R. Arndt, and Besser, as they are seen in the cortex of the cerebrum. They appear, however, to occur but rarely. The numerous anastomoses supposed to take place between the large ganglion cells in the nuclei of origin of various nerves in the spinal cord and medulla oblongata, and depicted amongst others by Schröder v. der Kolk and Lenhossek, have long been recognised as illusions. Other anastomoses between the ganglion cells of the various cortical layers of the brain, which are stated to occur by Meynert, require further corroboration. It is quite a matter of doubt whether

* Müller's *Archiv*, 1846, p. 317, Taf. 10.

† Arnold, in Virchow's *Archiv*, Band xli., Taf. 4.

we shall ever be able to observe those anastomoses between ganglion cells which result from the union of the finest outrunners of the branched processes, since the most carefully conducted methods of isolation adopted by Deiters have only led to negative results. Nor have my own numerous researches on the ganglion cells of the electric lobes of the torpedo, which are admirably adapted for this investigation, been more fortunate; for although Rud. Wagner long ago stated that anastomoses could here be distinctly seen, I, notwithstanding the employment of better modes of isolation, have been unable to discover a single instance of their occurrence. Lastly, an interesting accession to our knowledge of the terminations of the nerves may here be noted, with which I have become acquainted whilst these sheets were passing through the press. Paul Langerhans found, as he has described in Virchow's *Archiv*, Band xliv., p. 325, and depicted in the twelfth plate of that volume, that processes of the non-medullated fibres of the cutis in man penetrate between the cells of the rete Malpighii, exactly in the same way as has been described (p. 164) by Hoyer and Cohnheim as the mode of termination of the nerves in the cornea. These nerve fibrils, however, do not terminate by free extremities; but enter, as is rendered highly probable by Langerhans, in all instances, into small cells lying between the deeper cells of the rete mucosum, which again give off several fine fibrous outrunners into the upper layers; and these finally terminate with slightly clubbed extremities just beneath the horny layer. These nerve fibres have no connection with the tactile corpuscles. By means of these observations, which supplement those of Tomsa and others respecting the mode of termination of the nerves in the corium in several important particulars, the intimate connection between the terminations of the nerves and the epithelial layers in the skin of man has been demonstrated, which, since the year 1856, has been gradually shown to occur in all the other organs of sense, although it was in the first instance received with so much mistrust. Thus one more argument in favour of nerve plexuses representing the terminal structure falls to the ground.

CHAPTER IV.

THE TISSUE OF THE ORGANIC MUSCLES.

By J. ARNOLD.

The constituents of this tissue are fusiform contractile fibres, connective tissue, and cement, with vessels and nerves.

Form and general characteristics.—Fusiform fibres of this tissue are sometimes designated as smooth muscular fibres, or as contractile or muscular fibre cells; and when examined in an isolated and uncontracted condition, appear as sub-cylindrical fibres, generally with two or more flattened sides, and occasionally in the form of flattened oval plates. They for the most part resemble a spindle, being slightly swollen near the centre, and pointed towards each extremity (fig. 31, *a*); but the thickest part is frequently not quite centrally situated, being nearer to one end than to the other (fig. 31, *b*).

In many instances the extremities of the fibres are not single, but more or less divided, so that processes are given off from one or both poles; and in accordance with the depth to which the division extends, the length, form, and relative position of these processes vary (fig. 31, *c*). Thus, when the depth is slight, they are small, short, and more or less parallel to one another; when, on the other hand, it is considerable, they are long, broad, and diverge from each other almost at right angles. This forking of the muscular fibres occurs especially in those places where the fasciculi are arranged in the form of a network, and may properly be regarded as peculiar to this variety of the tissue. Such fibres, at all events, occur very frequently in the urinary bladder of the frog, at the points of intersection of the fasciculi.

The surfaces of the muscular fibres, as well as their borders, are generally smooth; the latter are, however, occasionally

Fig. 31.

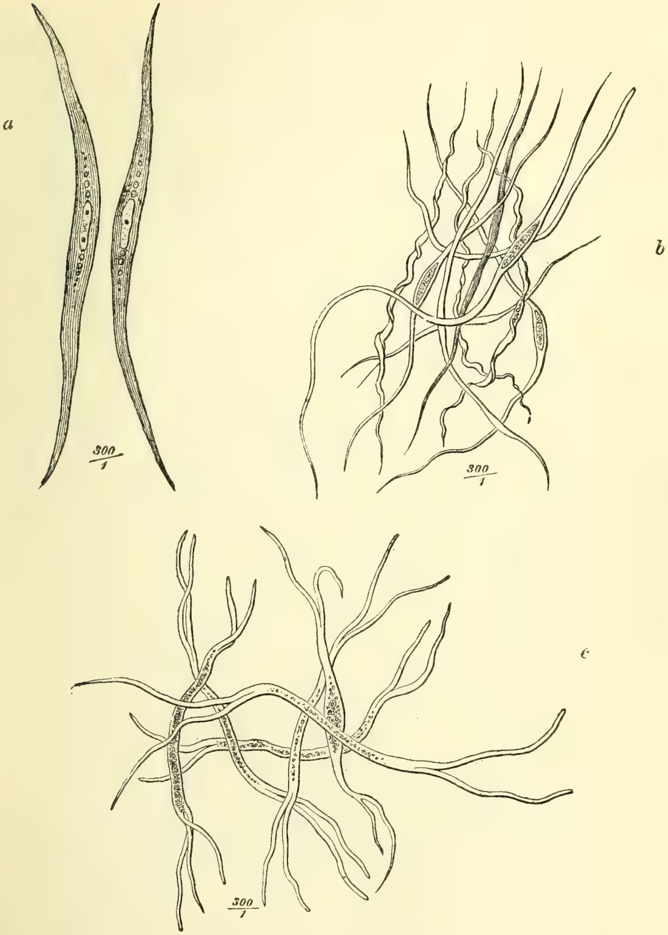

Fig. 31. *a*, Muscular fibres treated with serum; *b*, muscular fibres from the muscular tissue of the intestine, isolated by means of nitric acid; *c*, dichotomously divided muscular fibres from a pleuritic membrane.

slightly serrated, and the former are sometimes uneven,—appearances which, like the curving of the ends, must be regarded as consequences either of manipulation in the preparation of the specimen, or as *post-mortem* changes.

Another explanation must, however, be given of the transverse striæ, which occur in considerable numbers, and at regular distances, on one or both sides of the fibres. These, from the concordant results of the observations of Meissner* and Heidenhain,† are probably to be regarded as phenomena of contraction.

The length of the fibres varies from 0·045—0·230 millimeters; the mean length is from 0·048—0·089 millimeters; the breadth 0·004—0·01 millimeters.

Structure of the smooth Muscular Fibres.

The substance of the muscular fibre cells examined in serum whilst perfectly fresh has a dull appearance, except at the edges, which are frequently somewhat clearer. In many specimens no further indications of structure are perceptible, but in others there is a more or less distinct longitudinal striation, which is often particularly obvious near the extremities, and is rendered still clearer by the addition of a few drops of a 0·01 per cent. solution of chromic acid, or of solution of gold containing 0·1 per cent. (fig. 31, *a*). In many fibres, dark, highly refractile granules are imbedded in various parts, apparently without any definite arrangement. These, which disappear on the addition of alcohol, are not to be confounded with the granules that are commonly found at the two ends of the nucleus. The latter form pyramidal rows extending for a greater or less distance from the poles of the nucleus to which their bases are applied towards the ends of the fibres to which their apices point. These granules are imbedded in a substance which has likewise the form of a pyramid, and is differentiated from the adjoining material by its greater transparency when examined by transmitted light. In many fibres a second line is to be observed, which lies at some distance from, and not

* *Zeitschrift für rationelle Medicin*, Band ii., 1858.

† *Studien des Physiologischen Instituts*, 1861.

quite parallel to, the margin. This forms the line of demarcation between an external darker and an internal clearer and brighter layer. A similar differentiation of parts may be discerned on examining the transverse section of a fibre in which the cortical layer appears as a dark ring investing the remaining brighter portion. The outer contour of this is always distinctly marked, but its inner is never very sharply defined. The thickness of the cortical layer varies, and in many fibres it is altogether absent.

Margo* gave a description of certain small points arranged serially in the interior of the fibre cells, and separated from each other by minute intervals; whilst Wagener† first described the distinct longitudinal striation that gives the impression of a fibrillar arrangement near the extremities of the fibres. The rows of granules extending from the poles of the nucleus were first mentioned by Klebs,‡ and subsequently by Frankenhäuser§ and Wagener.||

NUCLEUS.—*General form and size.*—The nucleus of the fibre cells is generally single, very rarely multiple, always distinctly rod-shaped, and either rounded at the ends or pointed. It is occasionally curved or spirally convoluted. On transverse section the nucleus appears either round or subangular. It invariably occupies the fusiform enlargement of the fibre, but its position in regard to the transverse diameter is less constant, since on section it is sometimes seen to lie in the middle of the ring formed by the transverse section of the fibre, and sometimes near the margin. Moreover, the nucleus sometimes lies obliquely in relation to the axis of the fibre cell. The length of the nucleus varies from 0·015—0·022 millimeters, and its diameter from 0·002—0·003 millimeters.

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* *Neue Untersuchungen über die Entwickelung, das Wachsthum und den Bau der Muskelfasern,* "Recent Investigations on the Development, Growth, and Structure of Muscular Fibres," 1859.

† *Sitzungsberichte der Gesellschaft zur Beförderung der gesammten Naturwissenschaften,* No. 10, 1859.

‡ Virchow's *Archiv,* Band xxxii., 1865.

§ *Die Nerven der Gebärmutter und ihre Endigungen in den Glatten Muskelfasern,* "The Nerves of the Uterus, and their Mode of Termination in smooth Muscular Fibres," 1867.

|| *Loc. cit.*

Structure of the Nucleus.—In perfectly fresh muscular fibres treated with serum the nucleus may indeed be perceived, but its contour is not very well defined; on the addition, however, either of chromic acid (0·01 per cent.), acetic acid (1 per cent.), or solution of chloride of gold (0·1 per cent.), the contours become sharp and dark, whilst the previously homogeneous contents appear finely granular. In the substance of many nuclei, especially when treated with serum and chloride of gold, but less distinctly with acetic acid, there may be observed from two to four large (from 0·001—0·002 millimeters) highly refractile round granules (fig. 31, *a*). If one only be present, it lies near the centre, or frequently somewhat nearer to one of the poles of the nucleus. If, on the other hand, two are present, they are situated at the two ends of the nucleus. These granules are most distinct in transverse sections of the nucleus, and are then seldom absent. They may also be perceived in association with isolated nuclei, and in such cases they either lie close to the surface of the latter, or project more or less from its margin.

Frankenhäuser* has paid particular attention to the structure of the nucleus; and although Hessling† had previously noted the existence of a nucleolus in the interior of the nucleus, Frankenhäuser first stated that it was an essential and a never-failing constituent. Piso-Borme‡ also observed the presence of nucleoli.

Connection and Arrangement.—The contractile fibre cells are united into fasciculi or membranes of various size, through the intervention of a connecting material. The fibres are so arranged that the ends of two or more are inserted between the diverging extremities of two which touch at their dilated middle portion, an arrangement by which an intimate union of the several structures is effected. In cases where the greater number of the fibres are superimposed by their flat surfaces, a membrane is formed, consisting of one or many layers, the fibres for the most part preserving the same direction in

* *Loc. cit.*

† *Gewebelehre*, 1866.

‡ Moleschott's *Untersuchungen*, Band ix., 1860.

each layer, though they may pursue very different directions if several layers be present. Where the fibres are united, not in one, but in several directions, fasciculi of fibres are produced. These vary in length and thickness, and either run parallel to each other, or cross at a more or less acute angle, or, lastly, present a plexiform arrangement, and frequently anastomose. It is from these differences in the directions taken by the fibres, and in their mode of union, that the irregularities observed in section result. For if the section be carried transversely through a portion of the tissue in which the muscular fibres run parallel, round or subangular rings, lying in close proximity, are met with, presenting a central or laterally situated transversely divided nucleus; whilst if the bundles of fibres run in various

Fig. 32.

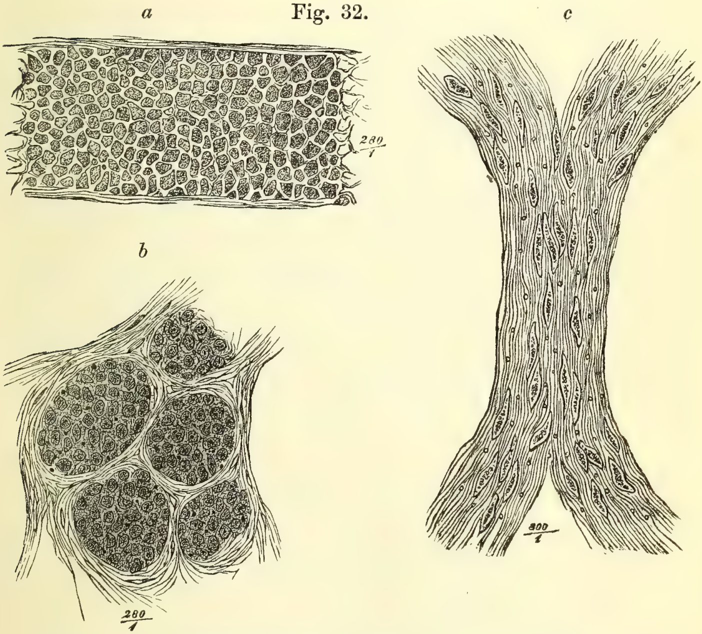

Fig. 32. *a*, Transverse section of the longitudinal fibrous layer of the intestine of a Frog; *b*, transverse section of muscular bundles from the uterus of a Sheep; *c*, muscular trabeculæ from the urinary bladder of a Frog, treated with acetic acid.

directions, transverse and oblique sections of the fibres and nuclei appear (fig. 32, *a* and *b*). The quantity of connecting substance is sometimes very sparing, so that the surfaces of the fibres are in almost direct contact, or are separated only by very thin layers or columns of the connecting substance. Occasionally, however, it is more abundant. In the former case the muscular fibres appear, on transverse section, as closely compressed polygonal areas; in the latter, as roundish spaces, between which are more or less broad laminæ of the connecting substance. This material is homogeneous, except that it contains numerous pale branched cells, the processes of which intercommunicate, and also a moderate number of dark, highly refractile granules, 0·001 to 0·002 millimeters in diameter, which are always visible. They sometimes lie in the centre of the connecting material, sometimes close to the borders of the spindle-like expansion of the fibre cells. They closely resemble the granules of the nucleus. In specimens treated with solutions of chloride of gold they present a dark violet tint, and are always much darker than other parts of the connecting substance (fig. 32, *c*).

Both the muscular fasciculi and the membranous expansions are invested both externally and internally by connective tissue, which, for the most part, is distinctly fibrillar, and contains loose fibres of connective and elastic tissue. By means of this the several laminæ are united into a membrane, and the fibres into fasciculi. The latter are sometimes so combined as to form a tough, dense, flattened or roundish mass, which, as Treitz* has shown, fulfils the office of a tendon.

VESSELS.—The layers of the connective tissue investing the fasciculi and membranes of organic muscular tissue, are traversed by numerous arteries of various size, which break up into a network of capillaries, from which again the veins take origin. These, like the arteries, run in the investing connective tissue; but the capillaries penetrate the muscular layers. The meshes of the capillary plexus are of moderate width, and are

* *Prager Vierteljahresschrift*, Band i., 1852.

sometimes elongated, and at others round or rhomboidal. The vessels themselves present no important peculiarities.

NERVES.—In all organs or parts of organs, in the composition of which the organic muscular tissue plays an important rôle, and apart from differences occurring in particular instances, a similar arrangement of the nerves is to be found. The different nerve fibres contain a variable number of dark-edged and pale nerve tubules. Of these, the former present the features characteristic of the medullated fibres, vary in size, and are usually the most abundant. There are, however, a few fasciculi, which chiefly consist of the pale fibres, and contain but a small number of the dark-edged variety. The former appear as fine glistening filaments, of from 0·0018 to 0·0023 millimeters in breadth, with here and there a nuclear enlargement of 0·003 to 0·005 millimeters in diameter, a peculiarity which at once enables them to be distinguished from even the finest doubly contoured fibre. The fasciculi thus composed of pale and dark-edged fibres, lie in the connective tissue surrounding the muscle bands or membranes, and form wide-meshed flat plexuses, in which the adjoining fibres cross and interchange from one plexiform layer into another. In the plexus formed by the larger nerves (*principal or fundamental plexus*) ganglion cells lie scattered, which are often collected into microscopic ganglia; and from the same plexus fibres are given off, which are at first dark edged, but subsequently assume the form of broad pale bands. These present a fine longitudinal striation, with nuclei at various distances, which are sometimes smaller than the fibres, and at others cause their edges to project. The pale fibres are from 0·004 to 0·005 millimeters in breadth, and their nuclei have about the same diameter. After running for a certain distance they rapidly diminish in size, and split into finer glistening fibres, which have nuclear enlargements and a diameter of from 0·0018 to 0·0023 millimeters, and are similar to those contained in the fasciculi. These fibres form plexuses with meshes of moderate size, and of rhomboidal or elongated shape. Bodies resembling nerve cells or nuclei with distinct nucleoli occupy the points of junction. Pale fibres, proceeding directly from the main or fundamental plexus, enter into this plexus. The

network of pale fibres, just described, lies immediately upon or beneath the muscular laminæ, embraces the muscular bundles, and probably intercommunicates freely with the fibres proceeding from the fundamental plexus to form an *intermediate plexus* (fig. 33, *b*). In the larger muscular fasciculi, portions of the intermediate plexus are sometimes found within the layers; but in general the arrangement above described is that which obtains. Fine fibres are given off from the intermediate plexus, which penetrate between the muscular fibres, and at the points of division still present nuclear enlargements, though these are subsequently absent, the fibres at the same time becoming rapidly attenuated (fig. 33, *a*). After they have undergone repeated division, they appear as fine, cylindrical, dark filaments, of from 0·0003 to 0·0005 millimeters in diameter. These contain, both in their course and at their points of division, dark granules of round, elliptical, or polygonal form, which, by their somewhat larger size (0·001 to 0·0018 millimeters) and brighter appearance, serve to indicate the course of the fibres (fig. 33, *a* and *b*). They are tolerably distinct in preparations moistened with serum; but, as has already been stated in the description of the connecting substance, the delicate plexus formed by the fibres is not very perceptible without the addition of other reagents. The delicate fibres bearing nuclei, which have just been described, unite with one another to form very delicate networks, which traverse the connecting substance occupying the interstices of the muscular fibres, and are seen winding round the fibres in the form of delicate dark lines, interrupted with nuclear enlargements, and constitute the *intra-muscular plexus*. Transverse sections of frozen portions of muscle treated with serum and chloride of gold permit these fine nuclei-bearing fibres, with their relations to the connecting substance on the one hand, and with the muscular fibres on the other, to be readily perceived (fig. 33, *c*). From the intra-muscular plexus, and chiefly in the vicinity of the spindle-like enlargements of the muscular fibres, dark peculiarly stiff filaments proceed, having a diameter of 0·00015 to 0·0002 millimeters. These penetrate into the interior of the fibres, and extend towards the nucleus. Several of these filaments, or one only, in accordance with the number of granules in the nucleus, may penetrate

a Fig. 33.

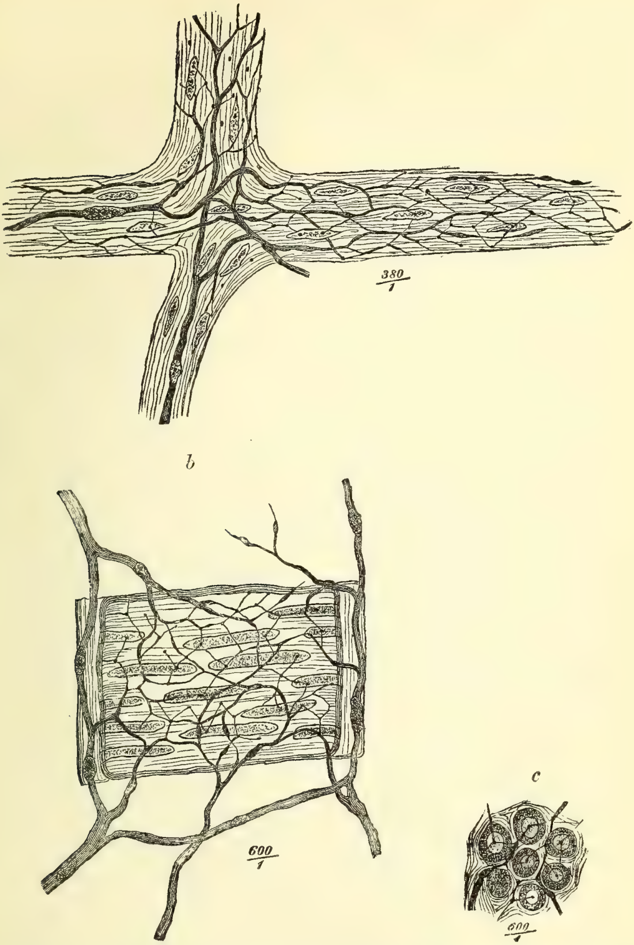

Fig. 33. Nerve ramifications and terminations in a muscular fasciculus taken from the urinary bladder of the Frog (prepared in chloride of gold solution); *b*, nerve ramification in the muscular coat of a small artery (prepared in acetic acid, 1 per cent., and chromic acid, 1-100th per cent.; *c*, ramification of the nerve, as shown on a transverse section of muscular fasciculi from the uterus of a Sheep. (The section was made from a portion of frozen muscle which had afterwards been treated with 0·01 per cent. of chromic acid.)

the muscular fibre from different sides; but, whatever may be their number, they all pass towards the granules of the nucleus, which might therefore be regarded as the extremities of the fibres, were it not that in many cases they again give off filaments, which, traversing the substance of the nucleus and of the muscular fibre in the opposite direction, enter the intra-muscular plexus. Consequently these granules are not the free ends of the smallest nerve fibres, but only the nodal points of the finest nerve plexus lying within the nucleus. The best demonstration of these relations also is to be obtained from transverse sections (fig. 33, *c*).

After Klebs* had in the first instance recognised that an intimate relation existed between the finest nerve filaments and the substance of the muscular fibres, it was shown by Frankenhäuser† that the former penetrated into the interior of the latter, and proceeded to the granules of the nucleus, to which he applied the name of nuclear corpuscles (Nucleoli, Kernkörperchen). The statements above made are the result of careful investigations which I have elsewhere more fully reported. As regards the relations of the finest nerve filaments to the substance of the muscular fibre and its nucleus, as well as to the intra-nuclear granules, I coincide with Frankenhäuser. On the other hand, I was unable to recognise the actual extremities of the nerve fibres in the granules of the nucleus; they rather appear to me as nodal points of the finest nerve plexus lying in the interior of the nucleus.

DISTRIBUTION.—Smooth muscular fibres are widely distributed through the body. In the organs of respiration they are seen to form layers of circular fibres in the posterior wall of the trachea, and in the bronchi. Their presence in the walls of the alveoli of the lungs in man and mammals is still doubtful, being admitted by some observers, whilst it is denied by others. Muscular fibres are, however, certainly present in the alveoli of the lungs in infants, and in the lungsacs of the frog, salamander, and triton.

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* *Loc. cit.*

† *Die Nerven der Gebärmutter und ihre Endigungen in den Glatten Muskelfasern,* "The Nerves of the Uterus, and their Mode of Termination in smooth Muscular Fibres," 1867.

In the alimentary canal, smooth muscular fibres form membranes, which are to be found from the lower part of the œsophagus to the extremity of the large intestine. They also form a proper layer in the mucous membrane, the so-called *muscularis mucosa*, and in the small intestine extend from thence into the villi. The excretory ducts of many glands possess a proper muscular layer, as may be seen in the pancreatic duct of the Ox, Cat, Pigeon, and Carp.

According to Tobien, the ducts of all the salivary glands contain muscular fibres; but Kölliker only saw a few in Wharton's duct, and Henle but a few in Steno's duct; whilst, according to Eberth, they are not present in the ducts of the salivary glands generally.

Smooth muscular fibres are also found in the lymphatic glands, and in the spleen. Opinions are, however, divided in regard to the distribution of the muscular tissue in the latter. In man, muscular fibres are contained in the capsule of the spleen; and some also maintain that they are present in the trabeculæ. The quantity of smooth muscular fibres in the capsule of the spleen in various animals differs to a considerable extent. They are very abundant in the porpoise, hedgehog, dog, cat, pig, mole, rat, and rabbit, but exist only in small quantity in the ruminants and in apes. In the pig, dog, ass, sheep, rabbit, horse, hedgehog, guinea-pig, peccary, bat, and cat, again, nearly *all* the trabeculæ contain muscular fibres; but in some, as the ox, these fibres are only present in the more delicate trabeculæ. Smooth muscular fibres are also found in the walls of the gall bladder, in the cystic duct, and in the ductus communis choledochus. They constitute an essential portion of the middle coat of the vessels; they form connected laminæ and membranes in the parietes of the calyces and pelvis of the kidney, and of the ureters and urinary bladder. They are found beneath the mucous membrane of the prostatic and membranous portions of the urethra, both in the male and female. Smooth muscular fibres are widely distributed in the male sexual apparatus, entering into the composition of the vas deferens, the vesicula seminalis, the prostate, the corpora cavernosa, Cowper's glands, and parepididymis; between the tunica vaginalis communis, and propria, and in the dartos. In the female

sexual organs it occurs in the oviducts, in the broad and round and in the anterior and posterior ligaments of the uterus. It is by far the most important constituent of the uterus. In the vagina it forms an actual muscular membrane. Its presence in the ovaries, whilst admitted by some, is denied by others. Numerous smooth muscular fibres are found in the nipple and in the surrounding areola, also near the hair follicles, where they have received the name of arrectores pili; and in the sebaceous and sweat follicles. Finally, the presence of smooth muscular fibres in the ciliary muscle, effecting the contraction and dilatation of the iris, is to be noted, and I may also refer to the discovery of smooth muscular fibres in the membranes of the egg.

Methods of Investigation.—The more delicate points in the structure of organic muscular fibre are best demonstrated in preparations that have been treated with serum, chromic acid (0·01 per cent.), and solution of gold (0·1 per cent). The urinary bladder, lungs, and smaller arterial vessels of the frog may be particularly recommended as forming good material for examination; but for the isolation of the individual fibres without the application of any reagents, the muscular tunics of the intestine are most appropriate. The means usually employed to effect the separation of the elementary fibres are acetic acid diluted with from 3 to 5 per cent. of water, nitric acid (20 per cent.) and solutions of potash (32 per cent.), all of which act in the same way by dissolving the connecting substance, and thus enabling the muscular fibres to be isolated. Maceration in iodized serum, and in dilute chromic acid (0·01 to 0·05 per cent.), is in some cases very effective. For the preparation of transverse sections, alcohol, chromate of potash, and chromic acid—the last two being employed alternately—constitute excellent hardening agents. If it be desired to examine the muscular fibre in as fresh a state as possible, transverse sections may be prepared from frozen portions of muscle, which have then been placed in serum. Such sections are, moreover, well adapted for being treated with gold, silver, and dilute chromic acid solutions. The course and termination of the nerves are distinctly seen in preparations macerated for from two

to four minutes in 4 cub. centim. of a solution of acetic acid, containing from 0·5 to 1 per cent., and then for half an hour or more in 4 cub. centim. of a 0·01 per cent. of chromic acid. Besides this combined action of acetic and chromic acids, I can also recommend acetic acid and alcohol both for the investigation of gold preparations and of sections treated with solutions of gold and chromic acid. The best materials are the urinary bladder and the smaller arteries of the frog. For treating the sections, carmine, anilin, chloride of palladium (F. E. Schulze), and picric acid (Schwarz) may be employed.

CHAPTER V.

THE MODE OF TERMINATION OF NERVE FIBRE IN MUSCLE.

By W. KÜHNE.

We exercise control over our muscles through the agency of the nerves, and it is through the nerve paths alone that the will excites them to contract. The question therefore naturally arises, In what way do nerves terminate in muscle? Inquiries were made on this point long before instruments and modes of investigation could furnish any answer, and these led to ever new and ever unsatisfactory researches.

We now believe that we are able to perceive the direct continuity of the contractile with the nervous substance. Yet it may still happen that, in consequence of further improvements in our means of observation, that which we regard as certain may be shown to be illusory. Nevertheless, work is indispensable, and we must press on till we reach the point in the domain of morphology, in which order and law become the last expression of our knowledge. Up to the year 1840 all attempts to give a satisfactory account of the ultimate termination of the motor nerves failed. The admission of loop-like extremities in the muscle can only be regarded as an expression of ignorance, and of the impossibility of following the course of the nerves in muscle with clearness.

But suddenly and accidentally an unprejudiced observer, in investigating the interesting small Tardigrada, recognised nearly all that we know at the present time regarding the ends of the motor nerves. In 1840, Doyère discovered that the nerve applied itself to the muscular fibre by means of a conical enlargement. Both of these structures are destitute of sheaths or

investing membranes in the Tardigrada (or bear animalcules), and the nervous and muscular tissues thus come into direct contact.

The observation of Doyère long remained misunderstood, and passed into oblivion in consequence of the general acceptance of the view of Ernst Brücke and Joh. Müller, to the effect that the primitive nerve fibres undergo division between the muscular fibres. It was, indeed, completely forgotten when R. Wagner recognised with much discrimination the value of that mode of nerve termination which Savi first discovered in the electrical organs of the Torpedo, and applied it as a fact of general significance to all peripherically distributed nerves. It then first became intelligible how so small a number of nerve fibres as those which are ordinarily contained in a motor nerve can influence such a much larger number of muscular fibres. In a carefully written essay, Reichert showed that the pectoral cutaneous muscle of the Frog, which is composed of about 160 muscular fibres, receives only about six or seven primitive nerve fibres; but the proportion was no longer unintelligible when far more, in fact nearly 300, terminal fibres, proceeding from the division of the latter, could be proved to be present. Of these investigations, however, few or none were directed to the solution of the question respecting the proper termination of the nerves, but rather to their mode of division between the muscular fasciculi. The latter point lies beyond the limits of the present paper, and we shall therefore content ourselves with the description of what is of most importance in regard to it.

When thin transparent muscles or thin sections of muscles are examined, nerves of varying degrees of fineness may be seen, the course of which is seldom parallel, but frequently at right angles, to the direction of the fibres of the muscle. This is especially noticeable in regard to isolated nerve fibres, and to the terminal portions of such fibres. The muscles of different animals, and even the several muscles of the same animal, are very unequally supplied with nerves. In a few of the lower animals, as in Bowerbankia, the muscles appear to possess as many nerve as muscular fibres; in others, especially in Fishes, there are surprisingly few, whilst amongst the warm-blooded Vertebrata the muscles of the eye, as a general rule, contain but few more muscular fibres than primitive nerve fibres. If we start with

the assumption that every muscular fibre must be supplied with at least one nerve fibre, even if this be the result of division, it is obvious that the muscular apparatus of Fishes, divided as it is to so great an extent by tendinous intersections, and which as a consequence of the shortness of these fibres, contains in an equal volume many more individual muscular fibres to be supplied with nerves, than the long-fibred muscles of other classes, can receive only a smaller number of primitive nerve fibres. The Fish would indeed have to carry a weighty mass of nerves, were the relation between the two tissues the same as in Mammals. Hence, nowhere are so many divisions of the primitive nerve fibres to be so easily found as in the muscles of this class.

The large relative number of nerves distributed to the ocular muscles, and generally present in all the muscles of Mammals, but as it would appear especially in the muscles of Man, is very suggestive in regard to the exact regulation of their movements, for the uncommonly fine adjustment of the ocular muscles would be unattainable if the excitation of one nerve fibre had as a consequence the excitation of as great a number of muscle fibres as in the Frog, and still more as in the Fish. In regard to the general distribution of nerves, allusion may here be made to the well-known fact that considerable segments of every muscle may be met with in which no nerves are to be found, and that in particular the extremities of the muscles appear to be destitute of nerves for a considerable space. The muscles that are best adapted for the study of the mode of division of the nerves supplying them, are the musculus cutaneus pectoris of the Frog, and also the sartorius, the ocular and digital muscles, and the hyoglossus of the same animal; the ocular muscles of the Fish, and amongst mammals those of the Cat, and, above all, the thin muscles which extend from the vertebral column to the skin in the Snake. These may be examined almost whilst yet still living, and merely flattened by a covering glass, or after being rendered transparent by means of a 1 per cent. solution of hydrochloric acid.

After the discovery of Doyère had shown the mode of connection of nerves without sheaths, with similarly naked muscular bands, the question naturally arose from a purely morphological point of view, whether transversely striated muscle, which

is invested by a sarcolemma, and to which only nerves provided with sheaths are distributed, does not at some point allow the passage of these through the membrane. Still more strongly was the hypothesis respecting the continuity of the sheath of Schwann with the sarcolemma, or in other words, of the passage of the nerve fibre directly into the contractile substance, advanced by physiologists, thus leading the way to the establishment of all that has been discovered respecting the termination of motor nerves since the time of Doyère.

We shall commence with the transversely striated muscles, proceeding from the lower to the higher groups of animals, and leaving on one side, for the present, the relations existing in the unstriated fibres, and the still very incompletely known but apparently smooth muscular fibres of the worm, and other still more lowly organised Invertebrata.

The Mode of Termination of the Nerves in Invertebrata.

The striated muscles of the Articulata consist of completely closed cylindrical tubes of sarcolemma, the contents of which present the well-known appearance of a stage or ladder-like arrangement of superimposed disks of muscle prisms.* The muscle prisms are separated from each other in the transverse direction by a considerable amount, and in the longitudinal by a small amount, of homogeneous fluid material. All muscles, moreover, contain, besides those constituents which form the really contractile substance of the muscle, still another material that has some, though a less important, influence on the development of force. It is generally regarded as the remains of the original formative cells of the muscle, and is composed of nuclei with a distinctly double-contoured membrane, and transparent contents, often with nucleoli; of vesicles of various form, without definite investment; of granules; and lastly, of a finely granular pappy mass. These masses may be very variously distributed in

* The term "disks" was introduced into the description of muscle by Mr. Bowman. The same parts were designated by Rollett "chief-substance disks." The muscle prisms have been also, after Mr. Bowman, termed "sarcous elements."

the interior of muscles, sometimes appearing in the form of a few short striæ, scattered through all parts of the fibre; sometimes as long bands lying between the contractile substance and the sarcolemma; and often, also, filling the interior of a canal running through the whole length of the fibre. In many instances the muscles of Crustacea present these masses in the form of a complete cylindrical tunic lying between the sarcolemma and the muscular substance. The masses may again be entirely isolated, or may communicate through the entire muscular fibre; those which lie in the central canals sending off radial processes which run towards the surface to join with the superficial portions, whilst in those which lie immediately beneath the sarcolemma, the processes extend towards the extremities of the fibres, and thus come into contact with others.

The most appropriate objects for the examination of the mode in which nerves terminate, appear to be the muscles of insects, and amongst these the best are the muscles of the great black water beetle (Hydrophilus piceus), which is to be preferred to the nearly allied Dytiscus marginalis. Instead of the muscles of the legs, it is better to employ the large colourless fasciculi lying in the thorax, which are attached by broad processes to the internal wing-like apodemata of the coxæ. If the muscle be suddenly separated from both its attachments by scissors, we obtain a preparation which, either without any addition, or merely with the addition of a little of the blood of the beetle, or a drop of 0·5 per cent. solution of chloride of sodium, will present, after gentle manipulation with needles, many beautifully isolated muscular fibres. These fibres are quite free from connective tissue, and are only bound together by nerves and tracheæ, both of which can be torn across with the greatest facility. Amongst the nerves many extraordinarily thick primitive fibres are to be found, invested by a distinct membrane, beneath which are very pale vesicular, and in parts also very finely granular medullary sheaths, whilst the axial portions present a fibrillar structure. The thick nerve fibres undergo repeated division, rivalling in this respect the ramifications of the bloodvessels of higher animals, and send off finer and still finer branches to the muscular fibres, each of which contains an extraordinary number of ultimate terminations. It

may then be observed that the middle portions of the muscular fibres, at all points of their circumference, present rows of funnel-shaped processes forming little eminences of various size, the apices of which correspond to the points of entrance of the several branches of nerves. The latter appear in all instances to consist only of *a single axial fibril or axis cylinder*; but this may usually be seen to divide into two strongly diverging branches immediately beneath the apex of the nerve cone or eminence, and it may also be followed for a short distance into the interior of the eminence.

Fig. 34.

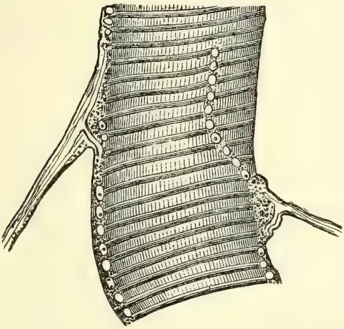

Fig. 34. Muscular fibre, with the extremities of two nerves, from the Hydrophilus piceus.

At the termination of the nerve the medullary layer, which has previously become extremely pale, entirely disappears; the image of the sheath of the nerve, therefore, where it joins the muscle, is not in the slightest degree obscured. It is impossible for the observer who sees this to doubt that the nerve sheath becomes continuous with the sarcolemma, and that the contour of the latter, as it rises towards the cone, or extends over the eminence, is directly continuous with the nerve sheath; or, in other words, that the nerve sheath and the sarcolemma form two communicating tubes. In whatever mode the nerve terminations may be presented to the eye, whether in a transverse section of the muscular fibre, or in the optic transverse section which is seen if a bent muscular fibre presents its convexity to the observer, he will still be constantly

led to the same conclusion. The forms that the nerve eminence may assume are very various, sometimes constituting a pointed cone, at others a low rounded elevation, whilst in others, again, it is almost flat,—varieties that are doubtless attributable to the traction which has been exerted in the nerve in the preparation of the specimen. Nevertheless we may sometimes see, if not the pointed limpet-like cones, yet elevations of considerable height on muscular fibres, whose nerves have not been disturbed, as well as in flat portions of muscles which have been removed from the surface with scissors. We may therefore apply the general term of nerve eminence to the whole nervous expansion at this point, and honour its discoverer by naming it the Doyèrian eminence. Wherever a nerve terminates, it will be found that the contractile substance is covered beneath the nerve eminence with the secondary constituents of the mass; that is, with nuclei, granules, molecules, and the like. This relation is perfectly intelligible in the case of those muscular fibres which possess an entire investment of this substance; but it is also found where the chief striæ of it do not lie immediately beneath the sarcolemma, but are present as a central axis only, in which case the latter forms a conical projection, that passes transversely through the contractile substance, and nearly reaches the apex of the Doyèrian eminence. In other cases, where elongated small masses are found immediately beneath the sarcolemma, these lose their otherwise straight form, and bulge upwards towards the nerve eminence. The eminence has in some instances only a single process, running in a longitudinal direction from its basis, but more frequently there are two, which pass in opposite directions. The termination of the axis cylinder in the eminence, and its usually forked division, does not appear to have been clearly recognised by the greater number of observers. Rouget considers that it terminates in the Crustacea in a blunt point at the line of junction of the granular nucleated mass with the contractile substance; whilst in Beetles, after a somewhat longer course, it terminates at the same point. It will not be possible, without further investigation, to decide the question in regard to the final disposition of the axis cylinder; for, however probable Rouget's

statements respecting the form that the process of the axis cylinder possesses may be, the position which he ascribes to it is, upon grounds that will hereafter be discussed, certainly surprising. The method of staining with solutions of gold and silver, which has been found so advantageous in other departments of the minute anatomy of the nerves, has up to the present, so far as this question is concerned at least, yielded no decisive results.

From what has already been stated it may, however, be maintained, in regard to the Arthropoda, that each of their muscular fibres receives a great number of nerve ends; that the nerve sheath is continuous with the sarcolemma; that the proper conducting nervous fibre, that is to say, the axis cylinder, traverses the point of union of the two tubes, and divides in the nerve eminence; and that all nerve eminences possess at their base a layer of protoplasmic muscle substance, that may stretch to a variable extent into the contractile part of the fibre. These results have been obtained from an examination of the tissues in Hydrophilus piceus, Dytiscus marginalis, Carabus auratus, Silpha obscura, Melolontha vulgaris, Geotrupes stercorarius, Trichodes apiarius and alvearius, Musca domestica, Tabanus bovinus, Bombus, Tegenaria, Argyroneta aquatica and Astacus fluviatilis, and consequently in all three classes of the Arthropoda.

The Mode of Termination of the Nerves in the Vertebrata.

A. *Amphibia.*—The knowledge of the mode of termination of the nerves in Amphibia, and especially in the Frog, is of great interest, because these animals have for so long a period been employed by physiologists as the subject of investigation in regard to the relations existing between motor nerves and muscles. The different muscles of the Frog which have been particularly examined are the sartorius, the muscles of the eye, the short fibres of the penniform gastrocnemius, and the small muscles of the foot that lie between the toes.

The uncontractile protoplasmic substance, or the remains of it, in the muscles of Frogs, occupies as is well known, a very

inconsiderable space, as compared with the transversely striated contractile material. The muscle fibres are, indeed, dotted with nuclei, which are found not only immediately beneath the sarcolemma, but in all parts of the transverse section; yet the protoplasmic portion is very small in quantity, and exists only in the form of a few molecules at the poles of the nuclei, or may even be altogether absent. Without methodical investigation it is almost impossible to strike upon the precise point in the fibres of the muscles of a frog which displays the mode of attachment of the nerve. This is sufficiently shown by the fruitless results of the observations repeatedly made antecedently to the last ten years.

After the experience that had been obtained respecting the connection of the nerves with the transversely striated muscular fibres invested with sarcolemma of the Invertebrata, it was somewhat more than an hypothesis when it was maintained that the conditions must be essentially similar in all animals in which nerves induce the act of contraction, and consequently in the Vertebrata. In order to decide whether every muscular fibre is connected with at least one nerve fibre, it was requisite to isolate the former in its whole length, and to examine its entire superficies. This was effected by the mode of isolating the fibres, suggested by Budge, through the agency of a mixture of chlorate of potash and nitric acid,—a plan that was advantageously modified by V. Wittich, who recommended that the muscle should be warmed with a very diluted solution of the same mixture. It is still better to soften the intermuscular connective tissue by maceration for twenty-four hours, in an extremely dilute solution of sulphuric acid, and subsequently to convert it into gelatine and effect its solution by warming it for a few hours at 104° Fahr. The isolation of the muscular fibres may then be accomplished by vigorous agitation with water in a test tube. By this method any muscle can be completely broken up into its individual fibres. The capillaries, which still often remain attached, must be removed by pencilling with a camel-hair brush. On carefully examining such isolated muscular fibres throughout their whole length, one spot at least may always be found to which a nerve fibre, usually more or less ramified, cleaves. In long

muscles—as, for example, the sartorius—many fibres may be found which present several such spots, whilst in the shorter fibres of the gastrocnemius, as a rule, only one nerve eminence is visible. In specimens prepared in this way the continuity of the nerve sheath of Schwann with the sarcolemma may be observed in profile, without any further manipulation.

In order to bring the termination of the nerves in the fresh, still living, and contractile muscle into view—as in the Arthropoda—the fibres of the gastrocnemius are to be isolated. In the broken-up and separated muscle the course of the finest nerve twigs, as they cross the fibres at right angles, may be followed without difficulty by the pigmented vessels that accompany them. In this region the terminal branches are given off; and if a few muscular fibres are raised with the forceps, after the tendinous fasciculi to which they are attached have been divided at both extremities, in all probability the desired appearances will be presented to the eye. The specimen so obtained may be examined, either without any addition or in a 0·5 per cent. solution of chloride of sodium, in which the muscle long retains its excitability. The aqueous humour and the serum of the blood of the frog may also be employed. Just before the nerve traverses the sarcolemma it usually undergoes division, forming the so-called terminal brush (leash or pencil) of the nerve, the extremely short branches of which seldom exceed in length the transverse diameter of the muscular fibre, and may lie in all conceivable directions to its axis. The number of branches of the first order rarely exceeds five; those of the second order may amount to ten or twelve. The medullary investment and the sheath of Schwann accompany the nerves up to the very point of their attachment to the muscular fibre, but here the medullary sheath terminates abruptly, and without marked attenuation. In profile views no kind of distinction is to be perceived between the contour of the sarcolemma and that of the membranous sheath; indeed, the flat and granulated nuclei of the latter can not unfrequently be followed into that part which all would acknowledge to be true sarcolemma, and which, as is well known, is in the frog destitute of nuclei. No better evidence than this can be offered in regard to the continuity of the two tubes.

At the point where the terminal nerve branches are abruptly given off, no elevation occurs in the frog, and only very rarely,

Fig. 35.

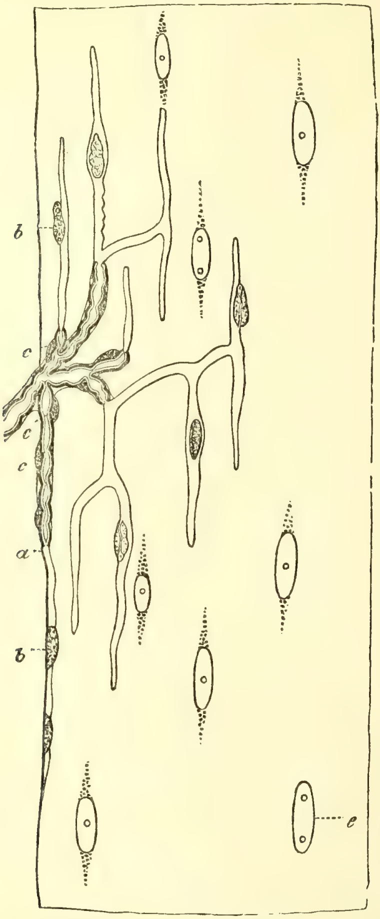

Fig. 35. Motor nerve terminations from the Frog. To avoid confusion, the transverse striæ of the muscular fibres are not indicated. At *a*, the passage of the nerve through the sarcolemma is seen in profile. The remaining portion of the intra-muscular cylinder axis expansion is more or less out of focus; *b b*, terminal nerve-bulbs; *c c c*, nuclei of the sheath of Schwann; *e*, nuclei of the muscle.

if the nerve has been forcibly stretched at the point where it appears to be most easily torn, does the medullary portion retract, so that a small empty funnel hangs over the border of the muscular fibre. Beneath the sarcolemma the nerves, now destitute of medullary sheaths, may be recognised in the form of small, moderately broad fibres, extending in a direction parallel to the muscular fibres, and often somewhat exceeding the breadth of the finest medullated branches. These fibres form a delicate pattern between the contractile substance and the sarcolemma, dividing and giving off branches of nearly equal breadth, from which again others course in a nearly parallel direction. The whole system which they form is usually three or four times longer than the transverse diameter of the muscular fibre. It never invests the whole circumference of the contractile substance, and the branches never penetrate far into the interior of it. There can be no question that we have here an intra-muscular branched expansion of the axis cylinder, and that it is the axial portion of the doubly contoured nerves which alone penetrates the sarcolemma, and forms beneath it a wide-meshed and in part fibrillated plexus. The fibres of the plexus appear to be in part round and partly flattened; they are very transparent, with delicate and for the most part smooth, though here and there finely serrated, contours.

Good instruments show with sufficient sharpness that the intra-muscular axis cylinders are not diffusely troubled or granular at their terminations. The actual extremity is always a distinctly rounded point. Here and there the axis cylinders are somewhat enlarged, and in such places small strongly granular corpuscles may usually be observed, the size of which is intermediate between those of the nuclei in the sheath of Schwann and the well-known muscle nuclei. They are pear-shaped, with the pointed extremity directed towards the end of the axis cylinder, and are found not only in the expanded portions of the latter, but occasionally in other parts, though always lying close to the axis cylinder. The finer structure of these *terminal nerve bulbs* may be well seen even with ordinary microscopic powers, but still better with a very strong objective and a low ocular. A fine tortuous fibre may then be observed to separate from the axis cylinder, which in

some places attains a considerable length, and, running along the bulb, terminates at its pointed end in a small swelling. This is all that has been ascertained up to the present time respecting the termination of the nerves in the Amphibia; the muscles of Tritons, Toads, the Proteus, and Salamanders presenting the same characters as those of the Frog. In these animals none of the granular and nucleated matrix is to be found which exists in the muscles of Arthropoda. A muscle nucleus with a small amount of protoplasm around it may, indeed, lie near the intra-muscular axis cylinder, but we never find at this point any special or peculiar disposition of this portion of the muscular contents. As regards the position of the terminal bulbs, as from their form these structures are named, they appear either to lie close to the nerves and on the same plane, or, as in the majority of instances, upon the latter and between them and the sarcolemma. Occasionally the author believes he has observed them to be absent. No physiological or morphological explanation has been advanced in respect to the significance of the nerve bulb; but it appears highly probable that the nuclei represent the earlier formative cells of the nerve and muscle, and consequently may be compared in some measure in their structure to the nuclei of the cells connected with nerves in the cutis of the tadpole that have been described by Hensen. According to this observer, the embryonic nerve fibres terminate in the nucleoli of these nucleated cells; the small pear-shaped knob at the end of the central fibre in the nerve bulbs would therefore correspond to the nucleoli.

Although there can be thus no doubt that in the Amphibia the nerve sheath is continuous with the sarcolemma, from whence it obviously follows that the contents of the former, if it extend beyond this point, must lie beneath the sarcolemma; yet this doctrine has received much opposition. The accuracy of the statements that have here been made may, however, be irrefragably proved by careful inquiry. The whole contents of the freshly isolated muscular fibre can be rendered fluid by hydrochloric acid of 1 per cent., whilst not only the primarily coagulated muscle plasma, but also the greater part of the muscle prisms, can be converted into a solution of syntonine. The entire contents of the muscle then, as is well known, move

easily hither and thither in the sarcolemma, if care be taken that the lumen of the latter remains open, and all pressure be avoided.

The intra-muscular axis cylinders of muscular fibres thus treated dissolve first at the points, then separate along their whole extent from the sarcolemma, and fall towards the centre of the tube, so that on shaking they float to and fro in the fluid. And there is yet another experiment which has led Cohnheim to the same result. He dipped fresh muscular fibres for a short time in acid, treated them with a weak solution of nitrate of silver, washed them with water, and allowed them to blacken in the light. A fine precipitate of silver occurred in the form of thin membranes between the muscle cylinder and the sarcolemma, which, after exposure to light, surrounded the muscular substance with a black layer beneath the sarcolemma. In this layer, stained with silver, the whole intra-muscular nervous apparatus appears as a white silhouette, indicating that something is here intercalated between the sarcolemma and the contractile substance, and this indeed is the intra-muscular axis cylinder. This experiment is interesting on several other accounts; for, in the first place, previous to the blackening taking place, the form of the nerve termination appears with surprising clearness, because the fine layer, composed of the silver precipitate, surrounds in the first instance everything that is of nervous nature with very distinct limiting lines; and, secondly, a means is obtained which is unfortunately the only one at present known, by which preparations of muscles exhibiting the mode of terminations of the nerves can, for a few months at least, be preserved. Lastly, it shows that there is present between the sarcolemma and the axis cylinder on the one hand, and between this and the contractile substance on the other, a capillary layer not capable of precipitation with a silver solution under the conditions which the experiment accidentally realizes, a something which is different from that which surrounds the whole contractile substance beneath the sarcolemma. The experiment of making the nerves float by treating the muscular tubes with diluted hydrochloric acid renders the former indeed probable; for it is then seen that the axis cylinder, beginning at the point, only gradually separates from the sarcolemma, to which it appears to be very firmly adherent; the

second method must at the same time appear still more important, because it indicates a more intimate connection between nerve and contractile substance than between this and the sarcolemma.

As regards the methods of investigation, it may here be added, that the greatest possible delicacy in manipulation is required, for the subject is one of the most difficult in the whole range of microscopic art, and is one also on which histologists are not, as yet, by any means unanimous, as the short historical sketch at the end of this article sufficiently shows. It is not sufficient to take the muscular fibre from still living and contractile muscles, but care must also be taken that, whilst still under the scrutiny of the observer, they retain their contractility, the covering glass being prevented by supports from exercising any pressure upon them. Fibres affected with rigor mortis are totally unserviceable, and also those which have had their axes rotated, or which have been in any way damaged. Maceration in acids that are at all concentrated leaves no vestige of the intra-muscular nerves beyond a few interrupted and broken striæ. Extremely dilute acids, as acetic acid of 0·5 per cent., or hydrochloric acid of 0·1 per cent., do not, indeed, render the image any clearer, but they do not destroy it; the terminal bulbs, however, soften under their influence in quite a peculiar manner, breaking up into a brush-like set of fibres; a change that stands in strong contrast to the well-known shrinking of the muscle nuclei and of the sheath of Schwann, and most distinctly proves the difference of the corpuscles of the axis cylinder from those structures.

The mode of termination of the nerves in Fishes has been hitherto but little investigated; by the application of some of the methods already adopted for the muscles of Amphibia, however, evidence has been obtained that here also the nerves penetrate the sarcolemma, and, at the point of entrance, lose their medullary sheath. The few extended investigations which have been instituted upon the mode of termination of the nerves in the Torpedo ocellata will be mentioned in the following paragraph.

B. *Reptiles, Birds, Mammals.*—In these animals also the mode of isolating the fibres by means of Budge's solution per-

mits the intimate union of the nerves with the muscular fibres to be proved; for, if the vascular network which contains the acid mixture have been removed with a brush, a short and frequently divided nerve stump often remains obstinately adherent to the fibre. An investigation by Rouget first led to exact conclusions in regard to the mode of termination of the nerves; since it demonstrated the existence of the Doyèrian eminence, in the first instance in lizards, and subsequently in warm-blooded animals. Rouget corroborated the statement he had already made, of the passage of the nerve through the sarcolemma, of the fusion of this with the sheath of Schwann, and added the important observation from his investigation of fresh muscle, such as can easily be obtained from Reptiles, that just beneath the point of entrance of the nerve, a mass of nuclei and granular substance, constituting a Doyèrian eminence, may be found exactly similar to that found in Arthropoda. And thus, although in the muscles of these animals there exists no such abundance of nucleated and protoplasmic formative material as in Arthropoda, yet this material is accumulated in greatest quantity immediately beneath the ends of the nerves. According to Rouget, the grumous mass, with the nuclei imbedded in it, constitutes the proper termination of the nerves, with which the axis cylinder becomes continuous, and thus modified, rests with a circular or elliptical flat basis on the contractile substance, the cylindrical mass of which it embraces for a certain distance, but never entirely surrounds. The rows of nuclei and of granular material that in Arthropoda extend for some distance along the muscle, are entirely absent in lizards and the warm-blooded vertebrates. The observation of Rouget soon received confirmation, and Krause appears to have been the first who correctly described and represented the nuclei of the nerve eminence, stating them to appear in the fresh muscle as small delicately contoured vesicles, with relatively large nucleoli; whilst, after the death of the muscle, and the addition of even very dilute acids, they become wrinkled and filled with granules. Rouget had only seen, and at a later period depicted them, when thus altered. The nuclei which are seen at the extremity of the nerve are, moreover, not all alike; one portion belonging to the eminence, and another to the

membrane which covers it; the latter being considerably smaller and flatter, rarely exhibiting a distinct nucleolus, and being always finely punctated or granular. As Krause has shown, they lie in the membrane, and may be regarded as the nuclei of the sheath of Schwann, where the latter, expanded over the eminence, is about to pass into the sarcolemma.

Nuclei presenting these characters are consequently only found upon the upper part of the eminence, so that their position alone renders it impossible to mistake them for the vesicular nuclei which are present only at the base of the eminence, or that portion of it which is directed towards the muscle. The small, hazy nuclei are distributed in far smaller number and irregularly in the membrane of the eminence, whilst the vesicular nuclei are arranged more or less definitely around the margin of the base. Finally, these small ellipsoids are placed with their long axis radially to the axis of the muscular fibre. They vary but slightly in size; in the lizards they are very little larger than the muscle nuclei, from which they are distinguished by their somewhat less elongated form, and by their presenting more rarely two nucleoli in their interior. In the warm-blooded animals, on the other hand, their size considerably exceeds that of the muscle nuclei.

The form of the nerve eminence in the muscles of Reptilia presents all conceivable varieties, being sometimes higher, and sometimes lower; sometimes having a long, elliptical, or even very extended basis; at others being nearly circular, or presenting the shape of a parallelogram with rounded angles. Those that are the most elongated are always the least prominent, forming, when the nerve end is seen in profile, scarcely any projection from the muscular fibre. In the warm-blooded animals, in which the nerve eminence is nearly circular, the eminence is likewise very flat,—relations which are here only alluded to, since they appear to be of subordinate importance.

The muscles of warm-blooded animals, as is well known, alter with great rapidity after death, and it is not surprising, therefore, that organs so delicate as the extremities of the nerves should likewise undergo cadaveric changes. Researches on the minute anatomy of these parts ought therefore to be commenced on Reptiles, whose muscles, especially at a low tempera-

ture, remain, like those of Amphibia, excitable for an astonishingly long period. It is, in truth, not difficult to recognise in lizards, as in Lacerta agilis and L. viridis, the mode in which the nerve terminates in the Doyèrian eminence. The granular mass, together with its nuclei, forms only the base or floor of the nerve end, whilst this is itself composed of a transparent non-granular plate, the *terminal nerve plate*, or the *motor nerve plate*.

At whatever period after death the muscles may be examined

Fig. 36.

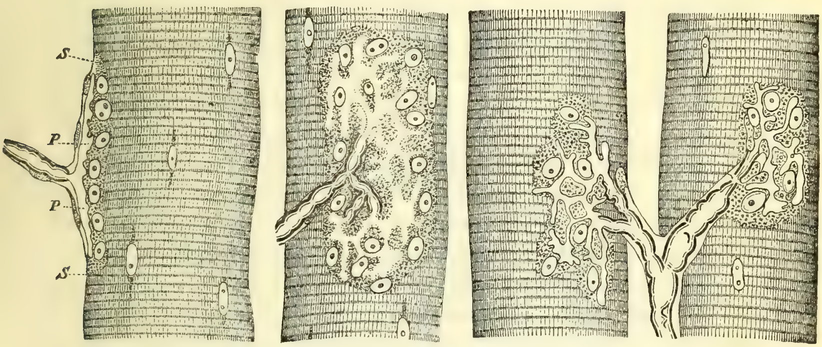

Fig. 36. Muscular fibres with nerve ends, from Lacerta viridis.

A. Seen in profile; *p p*, the terminal nerve plate; *s s*, the base or support of the plate, consisting of a granular mass with nuclei.

B. The same as seen in a perfectly fresh muscular fibre, whose nerve ends are still probably excitable; the delicate and pale contours which the frequently branched plate naturally possesses are not expressed in the woodcut.

C. The same as it appears after the death of the nerve end, as, for instance, two hours after poisoning with large doses of woorara.

there will always be found a third element in addition to those above named; namely, vesicles of various form, which are clear and transparent, pale contoured, and free from nucleoli; and these are to be found also in the nerve eminences of the warm-blooded animals. They are products of the very easily alterable nerve plate, probably acted on by the *post-mortem* formation of acid in the muscle.

Completely isolated muscular fibres removed from the still irritable thigh of a lizard, show characters which are almost

precisely similar to those of the frog; for though the muscular fibres are thicker, the nerve fasciculi are quite as much branched and divided. It is a matter of no difficulty, moreover, to find branches so placed that the point of entrance may be seen in profile; so that here also, from observations made on the perfectly fresh and living object, no doubt can exist in regard to the relations that exist between the nerve and muscle. The nerve plates can, on the other hand, be better surveyed and examined in face, enabling the nuclei to be well seen. A structure of beautiful form appears between these in pale bands, consisting of a delicate pattern of parallel lines, which sometimes form longer cords, sometimes sinuous plates, which are again perforated. If the muscle be tetanically contracted, the plates appear folded like the crop of a bird, their softly sinuous edges being angular and serrated. There may also be found at the periphery small delicate processes with club-like ends. Careful focussing with the microscope, with a profile view, shows that the terminal plate lies immediately beneath the membrane of the nerve eminence, and just above the granular mass; for it will be found that the greater number of bright nuclei first make their appearance on effecting the adjustment for depth. A few of the latter do, however, lie on the same plane as particular parts of the plate, where, for instance, they, with the granular mass surrounding them, occupy cavities in, or lie between, its folded borders. The above-described image is extraordinarily pale and delicate, and only a practised eye can recognise it in quite fresh and still contracting muscle. It is seen, for example, in the very thin cuticular muscles of the Coluber matrix, which can be placed under the microscope without preparation, and which present a few nerve ends supplying some of the fibres on their surface. Now inasmuch as these muscles contract through their whole extent when their nerves are irritated, and whilst still under observation, we may conclude with certainty that the pale and delicate image of the terminal plate represents truly the living condition, not only of the muscle, but of the nerve, whose termination it forms.

In those cases where the muscular fibre dies whilst in a state of rest, this image becomes continually clearer and sharper; whilst the contour of the plate, in the first instance, simply

becomes more clearly defined, without undergoing any essential change of form. But since portions of muscle thus excised rarely die in the condition of physiological rest, but become tetanically contracted before the occurrence of rigor mortis, and are then fixed in this condition by coagulation, it is comparatively rare to meet with the earliest stage in which the image is best shown. It is advantageous, therefore, to permit the muscles to die out in the dead body, and to examine them before they are so much stiffened as to become cloudy and opaque It appears, therefore, that the most distinct definition of the plates occurs previously to the death of the muscle, and especially at the time of the death of the nerve in the stage known to physiologists as that in which the muscle can no longer be excited to contract through the nerves, but is still capable of responding to direct stimulation. This condition, in which the muscle long retains its irritability, may, as is well known, be induced by poisoning with woorara, if the poison be given in large quantities, and be allowed to act for a sufficiently long period to produce evident paralysis of the terminal extremities of the motor nerves. Muscles that have thus been poisoned present in a distinctly marked manner an increased sharpness of contour of the terminal nerve plate—an appearance which may consequently be regarded as the outward and visible sign o commencing paralysis. This may perhaps be the result of a slight contraction of the plate, or of an inappreciable retraction of the granulated basis from the borders of the plate, which is nevertheless sufficient to induce the alteration in the image that we observe.

In the perfectly stiffened muscle, when its reaction has become acid, the contours of the plates change their form; the terminal nerve organ becoming continuously more and more folded and notched, and at length divided off into spherical masses, vesicles, or other forms, which are sometimes most remarkable. The whole of these changes may also be quickly induced by the action of very dilute acids; so that, in point of fact, no difference is observable from the ordinary cadaveric appearances, especially if, in order to dilute the acids, serum instead of water be employed, which prevents imbibition from taking place. This is, perhaps, a proof that the later cadaveric

changes of the terminal plate of the nerve depend on the *post-mortem* acidification of the muscle.

What has been already stated in reference to the muscles of Lizards and Snakes is equally applicable to those of warm-blooded animals, and also to those of Man. It is, indeed, scarcely possible to break up human muscles under the microscope in so fresh a condition that they may still be excited by irritation of their nerves, but they may be obtained so well preserved from amputated limbs that the terminal plate can be demonstrated with its nerve eminence but little altered, or, at all events, not separated into distinct masses by a process of constriction. The plates can be immediately seen in the muscles of Mammals and Birds, only these should be prevented from becoming too rapidly stiffened; and this may easily be accomplished by lowering the temperature of the preparation to 32° Fahr., and the addition of serum at the same temperature on cooled slides. With the rigidity which here always supervenes on the tetanic condition, the object ceases to be available for investigation, chiefly on account of the deeper-lying fibres of the muscle becoming too opaque; and as the terminations of the motor nerves in these animals become paralysed instantaneously after the cessation of the circulation of the blood through them, it follows that, even in the freshest condition of preparations taken from warm-blooded animals, the plates do not present very sharp outlines.

The determination of the thickness of the terminal plate and its relations to the adjoining parts, are points that demand methodical investigation. In the small nerve eminences of slender muscular fibres it presents itself when examined in profile as a thin mass projecting externally into the medullated nerve fibre somewhat in the form of a cone, with a sinuous inferior border, which is turned twards the basal substance or matrix on which it rests throughout its whole extent, and by which, as by a layer equal to itself in thickness, it is separated from the contractile substance. In accurately made transverse sections of the frozen muscles of Lizards, it appears, on the other hand, in the form of an irregularly reniform mass which at some points at least, gives the impression of being directly superimposed upon the muscular prisms. Such preparations remove every doubt respecting the relative position of th

contractile substance, the granular substance of the nerve eminence, the nerve plates, and the sarcolemma, which undoubtedly lie in that order from within outwards. Moreover, transverse sections of frozen muscles with their nerve eminences afford an insight into the thickness of the nerve plates. They show that this, as a whole, is not inconsiderable; that in the central part it is nearly as large as the short diameter of a nucleus of the basis substance, though at the edges and irregular processes it is far smaller; so that were it not for their transparency the transverse sections of these parts might be mistaken for granules of the basis.

Preparations made with osmic acid stain the nerves as far as the apex of the nerve eminence of a bluish black colour, whilst the contractile substance, the nerve plate, and the basis substance assume a clear yellow tint, and fat molecules in the muscle become brown,—reactions which prove that the whole intra-muscular nerve termination loses the characteristic constituents of the nerve medulla. The terminal nerve plate can be brought into view in an isolated condition, though certainly not situated externally to the muscle, without other addition than clear muscle serum. Isolated muscular fibres from the lizard, fixed under a covering glass, frequently exhibit, when they are in a complete state of rigor mortis, such contractions of the muscle coagulum, that large balls of this material accumulate in swollen portions of the sarcolemma, between other smaller spaces, filled only with muscle serum. If the last-mentioned empty spaces happen to occur at the place of the nerve entrance, the plate hangs free in the lumen of the sarcolemma, and it is deserving of notice that it even then still adheres to the protoplasmic substance and nuclei which constitute the basal substance of the nerve eminence. It appears, therefore, that further investigation is requisite to enable a positive statement to be made in regard to the union that exists between the two constituents of the nerve eminence.

From what has been now advanced, we may conclude, then, that the appearances presented by the extremities of the motor nerves are so various that scarcely any scheme can at present be constructed that shall give a representation, the morphological and physiological features of which shall be applicable to all animals.

According to Doyère, the pale, transparent, and non-granular nerve of Milnesium tardigradum becomes converted at the periphery into a finely granular eminence, which partly surrounds the equally pale, untroubled, and non-striated muscular fibre, and may extend a little distance along its border. These statements have been completely corroborated by renewed and very careful investigation of the Tardigrada (bear animalcules) by V. Greeff. This observer readily found the appearances so long known from Doyère's drawings, but also observed a small spherical nucleus to be constantly present in the little nerve eminence, with a few sparsely scattered somewhat larger nuclei, very sparingly surrounded by punctated protoplasm, adherent to the muscle, and which for the most part lie at a consider-

Fig. 37.

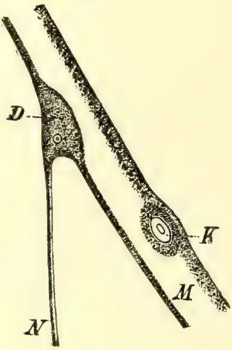

Fig. 37. Termination of a nerve in Milnesium tardigradum (one of the sloth or bear animalcules), according to Greeff. M, muscular fibre; K, nucleus of muscle; D, eminence of Doyère; N, nerve.

able distance from the termination of the nerve. V. Greeff was unable to find, either on the nerve or on the muscle, anything corresponding to the sheath of Schwann or to the sarcolemma.

Of those points which have been described by a few observers in respect to the termination of the nerves in the non-striated muscles of the lower animals, and in the smooth muscular tissue of the Vertebrata, mention has already been made under their appropriate heading. Trinchese has given some details respecting the termination of the nerves in the muscles, that

have hitherto been regarded as unstriated, of Helix pomatia and of Bowerbankia. According to him, a fine nerve fibril enters the large muscular fibre cells of the muscular apparatus of the foot of Helix pomatia near their centre, divides immediately in their interior into two branches, which extend to the two pointed ends of the muscular fibre in the form of two elongated, and towards their extremities spirally twisted, threads. In the centre, and just subjacent to the point of division, an ellipsoidal accumulation of finely granular substance exists. In Bowerbankia, whose muscles Trinchese likewise describes as smooth bands, only a low conical process of the somewhat broader nerve fibre is present, in which cone, and at its base where it touches the muscle, is the granular material with a spherical nucleus and nucleoli.

The question now arises, what is the essential nature of the termination of the motor nerve? The author cannot doubt that this is at present most imperfectly known in the Arthropoda. Rouget, indeed, states that he succeeded in perceiving a prolongation of the axis cylinder in the nerve eminence in the form of a system of branched fibres; and we must probably admit that this system does exist: but the further statement of Rouget, who attributes nervous properties to this part alone, as was generally previously admitted in Germany, and that this ramified system of fibres lies beneath the nucleated substratum, appears to the author to be very much in need of confirmation. Engelmann, who also examined the muscles of the Arthropoda, depicted a transparent homogeneous and quite vesicular mass at the apex of his nerve eminence, which appears to be the analogue of the terminal nerve plate found in Reptiles and Mammals, and, like these, to be bounded throughout the greater part of the surface turned towards the contractile substance by a granulated substratum. If this supposition be established —namely, that in the Arthropoda also a non-granular plate, or even a structure similar to the intra-muscular axis-cylinder system of the Amphibia is present, covering the granular nucleated substratum, to which Rouget's statements appear to point—we should have obtained the much-desired uniformity of structure; and there would then be *one* mode of nerve termination, in which the nerve ends with a motor plate in a

nerve eminence, resting on a nucleated bed of protoplasm or a matrix; and a *second* mode, in which, as in Amphibia, the matrix is absent, and the nerve ends in an elongated and branched fibre-like plate. Only the Amphibia possess terminal bulbs, the analogue of which Cohnheim stands alone in considering to be found in the plates of Lizards; that is to say, in the small granular sessile and more conical corpuscles that are found in these animals, respecting which further investigations are needed. Greeff first advanced the view that the mode of nerve termination in Milnesium may be assimilated to an expanded flat ganglion cell adherent to the muscular fibre; and were we to transfer this idea to the higher animals we should have to regard their nerves as terminating in a collection of ganglion cells, corresponding in number to the nuclei present, or in a ganglion cell containing many nuclei, or perhaps in a series of ganglion cells which have become fused together; that is to say, which have formed a ganglionic nerve plate. This view does not, however, materially advance our knowledge; for, even if it be correct, we shall have to seek for the minute anatomy of these terminal ganglion cells just as has been done for those of the nervous centres and others; and if we have already acquired a considerable amount of information respecting these, we yet know still more in regard to the nerves terminating in muscle, since we are acquainted with the plates, and their subjacent protoplasm, from which they are rarely sharply differentiated. We need not despair of discovering their analogue in all nerve eminences, even in the minute ones of Milnesium, though perhaps better instruments and improved methods of investigation will be required to discover the finer points of their structure than those we at present possess.

As long as the granular contents of the nerve eminence were regarded as the proper continuation of the axis cylinder, as it now is by Rouget, in the case of Mammals and Reptiles—though he does not perceive that this involves a contradiction to his former very decisive and explicit statements that in the Arthropoda his system of fibres was the only part of a truly nervous nature, the remaining structures, *i.e.* the granular mass and the nuclei, being accessory—so long could the view be maintained that the nerve becomes directly continuous with the

contractile substance. This last idea is, however, opposed, from a morphological point of view, by a consideration of the mode of nerve termination in the frog; since, if there be a fact in the whole range of this inquiry capable of being easily ascertained, it is the invariably sharply defined and distinct termination of the intra-muscular axis cylinder in the Amphibia. That view is also, and has long been, opposed by physiological considerations; for it is demonstrable that the muscle does not act upon the nerve fibre, but that, on the contrary, all stimuli are conducted from the nerve to the muscle, and never in the inverse direction; and for this purpose the nerve termination forms, as we now know, the visible structure. It may indeed be that a finer series of radiating processes from the nerve plate may penetrate between the granules of the substratum than we are at present disposed to admit; and many circumstances may be adduced in favour of this supposition, as, for example, the intimate adhesion of the two parts to one another, even when the contents of the eminence no longer rest upon the muscle. It is obvious, then, that it remains to be shown that the substratum constitutes a direct transition to the contractile, since there are muscles, especially amongst the Amphibia, in which this structural characteristic is entirely absent.

The present state of our information upon these points may be shortly expressed as follows:—

In all transversely striated muscles the nerves terminate beneath the sarcolemma, the sheath of Schwann becoming continuous with the latter. Up to this point the axis cylinder is accompanied by the medullary sheath. The extremity of the axis cylinder always corresponds to a remarkably broad expansion, which constantly forms a flat branching mass. This terminal nerve plate sometimes presents the character of a membrane, and at others resembles a system of fibres. In the greater number of cases the plate rests upon a substratum of nuclei and finely granular protoplasm, whilst in others this material is absent, and the nerve plates possess the so-called terminal nerve bulbs. The extremity of the nerve never penetrates into the interior of the contractile cylinder, and, on the other hand, never entirely invests it. Short muscular fibres usually receive only one nerve; but long fibres have several.

We may add, hypothetically, that the substratum represents the remains of a formative material important in the development of both the muscular and nervous tissue, and that a similar explanation may be offered of the nature of the terminal nerve bulbs in respect to the nervous tissue.

History and Literature.—The preceding observations have been so ordered as to give the historical development of the principal facts with which we are at present acquainted respecting the modes in which nerves terminate in muscle. Those observers, therefore, that have contributed any essentially new information on the subject, have already been mentioned. A few remarks may, however, still be added, since the questions involved have given occasion to lively controversy during the last ten years.

In few departments of histology has methodically prosecuted investigation, proceeding always from hypothesis, proved more fruitful in results than in relation to the question of the connection existing between nerve and muscle. The modern science of morphology has undoubtedly reaped the value of that experience that has been obtained in all other branches of knowledge, in having become a special subject; and the example before us will serve, perhaps, to point out the advantages that histology, which inclines as much towards morphology as towards physiology, has to anticipate from hypotheses borrowed from both departments.

We shall here leave unnoticed the older works, so far, at least, as they bear upon the unsatisfactory view of nerve loops.

In the same year that Savi (2) communicated his important observations of the division of the primitive nerve fibres in the electric organs of the Torpedo to a scientific congress at Florence, Doyère (1) discovered the termination of the motor nerves in Milnesium tardigradum. Remak (3) then incidentally stated that in mammals the nerves appeared to him to end in a plexus of pale fibres, winding around the external surface of the sarcolemma. Quatrefages (4) verified the discovery of Doyère in the case of Eolidina. In 1844, E. Brücke and Joh. Müller first observed the division of primitive nerve fibres in the muscles of the eye of the pike, and R. Wagner (6) observed the same thing in the musculus hyoideus of the frog. Kölliker (7) soon after established the Doyèrian mode of termination of the nerves in the larva of Chironomus, and Reichert (8) demonstrated the division in the cutaneous muscle of the thorax in the frog, where he found by direct counting that a few nerve fibres furnish more branches than the number of the muscular fibres to be supplied. The

Doyèrian mode of termination was again corroborated by Meissner (9), in Mermis and Ascaris, and by Wedl (10), Walther (11), and Munk (12), in several Nematodes. At a somewhat later period, Schaafhausen expressed himself in terms similar to those of Remak, and believed that he had seen a fine network of fibres, tinted with carmine, investing the whole muscular fibre. At this date the above-described mode of termination of the nerves in the muscles of insects was discovered (14, 15), and inasmuch as the nerves were here proved to terminate beneath the sarcolemma in muscles possessing this membrane, the view entertained by Schaafhausen respecting the similarly constructed muscles of vertebrate animals was rendered improbable. Nevertheless, a similar conclusion was arrived at by Beale (16, 17), an energetic inquirer who maintained that in the frog in particular the nerves gave off relatively broad nucleated fibres. Since, however, he did not adopt the method of isolation, but coloured his preparations deeply with carmine, it is possible he may have been deceived by the confusion of fibres traversing the accessory structures associated with muscle. Investigations undertaken upon isolated muscular fibres from the frog (18, 20) now led to the discovery of the intra-muscular axis cylinder and its terminal bulbs. The penetration of the nerve through the sarcolemma, now for the first time demonstrated, was established by Margo (19), who considered the axis cylinder terminated in a system of nucleated and granulated fibres which penetrated the contractile substance to all depths. The views of Margo, which he subsequently extended to the Arthropoda (27), have never found adherents, since they clearly rested on illusory appearances caused by the well-known serially arranged interstitial granules which are present in so many muscles. In the meanwhile Kölliker reverted to the views of Beale, but with the addition that he regarded the nerves as frequently exhibiting free extremities, and did not, as Beale thought, form a completely closed plexus. Resting on this assumption, Kölliker, who undoubtedly first rediscovered the intra-muscular axis cylinder of the frog (25, 26), maintained that the terminal bulbs there seen were really nuclei of the sheath of Schwann. Krause (24) and Rouget (29) agreed with him in all points, and now, whilst Beale (28) retained his first opinion as being applicable to all classes of animals, Rouget (29) came forward with his discovery of the nerve eminence in reptiles and warm-blooded animals, and was corroborated in all essential particulars by Krause (31), Engelmann (34, 38), and the author (39, 40); by the latter, indeed, with special emphasis, because Krause had given quite a different signification to the nerve eminence; had

placed it external to the sarcolemma; had described the nuclei as being situated in the membrane, and the whole structure as being an organ more analogous to the nerve bulbs invested by the sac-like sheath of the nerve. The opposite views that Krause took on these points to the descriptions given by Rouget, Waldeyer (35), Letzerich (37), and Engelmann, were based on the application of uncertain methods of investigation, especially in the attempt to establish the presence of a sharply defined line belonging to the sarcolemma between the contractile substance and the substratum of the nerve plate which he obtained by the coagulation of the muscle in bichromate of potash, or by the examination of the transverse sections of dried muscle. The lines thus produced do, indeed, lie subjacent to the sarcolemma. It is conceivable that Krause, and perhaps also Letzerich, if the author rightly comprehends the latter, perceived in the nerve eminence the first indications of the nerve plate; that which Krause described as a pale terminal fibre ending in a bulb being a portion or an optical longitudinal section of the nerve plate, whilst that which Letzerich compared to fluid wax was the plate itself. Thus, in the first investigation on the muscles of Reptiles in Germany, the nerve plate was recognised (47) as the immediate and proper terminal organ of the axis cylinder, whilst it was at the same time established that the granulated and nucleated mass previously taken for it was only the substratum of the plate. That which Rouget, Engelmann, Waldeyer, and Krause regarded as the nerve plate, advantageously exchanged its name for that of nerve eminence (Doyère's cone), in order to preserve the otherwise very appropriate term of *terminal plate* for the true extremity of the nerve, which expresses well the peculiar form that it presents. The nerve plate was soon recognised as an essential constituent of the nerve eminence in the muscles of warm-blooded animals and of man (48). In the meantime Rouget (43) and Krause (41), in the case of the frog, pursuing the method suggested by Waldeyer, who also believed he had seen a nerve eminence in that animal, adopted another view, Krause describing in the muscles of the frog extremely minute nerve eminences which he believed to be situated externally to the sarcolemna, and to which long, pale, and delicate nerve fibres ran, whilst Rouget considered that the nerves ended by a blunt extremity at the sarcolemma, which was itself continuous with the sheath of Schwann. Neither a nerve eminence, nor any similar prolongation of the axis cylinder is present, according to Rouget, in the muscles of the frog. The true intra-muscular termination of the nerve again apparently escaped the observation of both observers; for

Krause, in preparations where the nerves had undergone much stretching, and had on that account become attenuated, mistook the point of attachment of the nerve which had thus been rendered conical with the ultimate nuclei of the sheath of Schwann for the nerve eminence; whilst Rouget obviously overlooked the entire expansion of the now no longer medullated nerve, after he had been accustomed to the infinitely more sharply defined images of the same parts in the muscles of lizards. In the meanwhile Engelmann (38) had been successful in discovering the elongated expansion of the axis cylinder in the frog, with the exception only that he denied the minute anatomy of the terminal bulbs, and believed a granular substratum to be here present, constituting an intermediate structure between nervous and contractile tissue, and continuous with both. The objections to this view, extended by Engelmann to the muscles of all animals, have been already adduced, and it need here only be added that his description of the granular mass in the frog is decidedly erroneous. The most satisfactory demonstration of the accuracy of the mode of termination of the nerves described in the text results from the application of the silver mode of preparation, and has been furnished by Cohnheim (46, 60); this mode is equally well adapted to display the terminal nerve plate in the Doyèrian eminence which comes into view in muscles blackened with silver, in the form of a beautiful white pattern. The same author has pointed out that the isolation of the nerves from the remains of the nerve eminence adherent to them, accomplished by Krause with the aid of moderately strong hydrochloric acid, is not to be regarded as a proof of the eminence being situated on the outer surface of the sarcolemma, because the acid under the conditions maintained by Krause, to wit, degree of concentration and duration of action, effects the solution of the sarcolemma, and consequently lays bare the muscle, and breaks down the continuity of the nerve with the muscular fibre. The existence of the terminal plate has still more recently been vigorously contested by Rouget (56) and Krause, who explain the whole appearance as a hitherto undescribed *post-mortem* phenomenon of coagulation, in contradiction to which, again, Rouget stated that the true termination of the axis cylinder in the nerve eminence consists in its metamorphosis into a granular mass with interspersed nuclei. Rouget soon again retracted this view for the muscles of Arthropoda, and especially for those of Crustacea, in which he discovered an analogue to the plate, or at least to the more fibrous mode of the termination of nerve fibres that occurs in the frog. It is reserved for further research to decide whether Rouget's statements are correct, to the effect that

this fibre system, in opposition to all analogy derived from the Vertebrata, penetrates the granulated substratum, and comes into direct contact with the contractile substance. Engelmann's observations (67), at all events, expressly establish the latter point.

To all appearance, the general results of inquiry upon the important question of the mode of termination of the motor nerves seem to show that the views of Remak, Beale, and Kölliker must generally be given up, whilst Rouget admits that in the case of Crustacea, at least, the axis cylinder does not terminate in a band-like and granular manner. It appears, lastly, from the very recent brief essay of Krause (64), that this author also has given up his two former views in respect to the muscles of Amphibia, and has now actually seen the fibre system of the intra-muscular axis cylinder, and also, by the application of the colouring method with solutions of gold, the exceedingly beautiful form of the nerve plate in the muscles of Lizards. The next step that has now to be taken in advance, is to interpret the relations of the lower surface of the plate to the granulated substratum. The author is unable to express an opinion upon the statements of Trinchese (63), which relate to the nerve eminence of the Torpedo. According to this observer, the nerves of this fish possess duplicate sheaths at their extremity, of which only the perineurium is continuous with the sarcolemma, whilst the nucleated sheath of Schwann accompanies the axis cylinder where it penetrates into the nerve eminence, and everywhere loosely invests the flat plexus formed by the division of the axis cylinder. Trinchese describes peculiar ganglionic enlargements on the thus modified axis cylinder, and true terminal ganglion cells, with nucleus and nucleoli, on the projecting extremities of the network; other nuclei distributed through the nerve eminence he refers to the sheath of Schwann contained in the muscle. The drawings of Trinchese, although taken from preparations materially modified by diluted hydrochloric acid, and undoubtedly deprived of their best qualities, show what excellent materials were at his disposal, and render it extremely probable that these animals present the most magnificent motor terminal plates in existence, though the delicacy and beauty of their form are lost in all but physiologically fresh specimens.

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CHAPTER VI.

THE BEHAVIOUR OF MUSCULAR FIBRES WHEN EXAMINED BY POLARISED LIGHT.

By E. BRÜCKE.

When muscular fibres are examined with a microscope to which a polarising apparatus is attached, remarkable and instructive phenomena are observed. If the field be darkened by crossing the planes of polarisation of the Nicol's prisms, those fibres only disappear which lie parallel to the plane of polarisation of one or other of the prisms; the rest, which cut those planes at various angles between 0° and 90°, appear of a grey colour upon a black ground, the most distinct being those which cut them at an angle of 45°. In those parts where the muscular fibres running parallel with one another are arranged in several layers, the colour assumes a whitish tint, passing into yellow. The tint varies with the thickness of the layers, precisely as the succession of colours in Newton's rings, from the centre towards the circumference. If one of the Nicol's prisms be turned to the extent of 90°, so that the field becomes clear, and attains its maximum brightness, the complementary tints make their appearance. These phenomena, with others that will presently be described, are equally apparent when the muscular fibres are thoroughly impregnated with, and surrounded by, strongly refracting fluids, as glycerine, turpentine, and Canada balsam. This is essentially owing to the circumstance that the muscle substance is doubly refractile, two systems of undulations propagating themselves according to different laws, and interfering the one with the other.

This explanation had already been given in 1839 by

Prof. C. Bœck,* of Christiania, who was the first that applied the polarising microscope to the investigation of animal and vegetable tissues; and no other intelligible explanation has since this period been advanced of the phenomena observed.

The next question to determine is, whether the entire substance of the muscular fibres possesses an equal power of double refraction, or whether it is possible to distinguish doubly refracting from isotropal parts. If sufficiently high magnifying powers are employed, and the observations be made on animals which have large sarcous elements, amongst which our large water-beetle, the Hydrophilus piceus, is the best, it will be immediately seen that only the sarcous elements are doubly refracting, and that the intervening material which separates them from one another is isotropal; for it remains dark in the dark field of the crossed Nicol's prisms, in whatever azimuth the muscular fibre to which it forms a part may be placed; it is just as dark in those muscular fibres which form an angle of 45° with the polarising planes of the prisms, as in those which make an angle of 0° or of 90° with those planes.

This becomes still more evident if a water-beetle be killed by immersion in strong alcohol, and after a few days' maceration the muscles of one of its thighs be placed in oil of turpentine, and finally in Canada balsam. Owing to the high refracting index of the balsam the muscular fibres appear in ordinary light very pale and transparent, and all the stronger shadows vanish; but on this very account all the phenomena caused by double refraction appear with corresponding distinctness under the polarising microscope. But in what way are the sarcous elements doubly refractile? Are they positive or negative? Are they uniaxial or biaxial?

If a transverse section of the muscle hardened in spirit be thoroughly impregnated with Canada balsam, and examined with the polarising apparatus, it will be found that as it is turned round the axis of the instrument a portion of the cut

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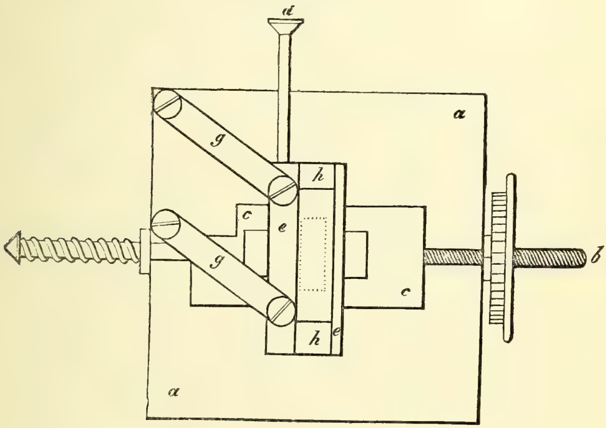
* *Transactions of the Scandinavian Society of Naturalists in Götheborg in* 1839, *and in Copenhagen in* 1840. *Report on the progress of Anatomy and Physiology in Scandinavian Literature in the years* 1840—1843, by Ad. Hannover, in J. Müller's *Archiv für Anatomie u. Physiologie*, 1844.

surface remains constantly dark in the dark field of the crossed Nicol's prism, whilst the remainder, in the effective azimuths—that is, in those in which they make angles between 0° and 45° with the planes of polarisation—become clear. It soon appears that such as always remain dark are those which lie exactly parallel to the axis of the instrument, whilst this is not the case with the rest. There is thus an optic axis precisely corresponding with the longitudinal direction of the muscular fibres. Now, inasmuch as this coincides with the longitudinal dimensions of the straight prisms represented by the sarcous elements, and since we are unable to discover a second optic axis, or

Fig. 38.



any indication of its existence, we must regard the sarcous elements as uniaxial.

Are they positively or negatively doubly refractile? In order to determine this I have constructed the instrument shown in the accompanying figure. The blackened brass plate *a a*, perforated in the centre, and connected to the object plate of the microscope, possesses two slides, which can be moved over one another; the lower *c c* by means of the micrometer screw *b*, the upper *e e* with the unassisted hand by means of the handle *d* on the parallelogram *g g*. Both slides carry prisms of quartz, the upper one movable

in the direction of its length in a groove *h h*; the lower one fixed, and only movable together with the slide by means of the micrometer screw. The prisms rest upon their thin edges, and the stage is perforated immediately beneath them, so that the light is freely transmitted. They have both a corresponding angle of 1° 6′ 54″, and are so cut that one of the inclined planes in each is parallel to the crystallographic principal axis, so placed that the light reflected from the mirror of the microscope passes perpendicularly to this axis in each, and so arranged that the two principal axes cross each other at right angles, each of them making an angle of 45° with the polarising plane of the subjacent Nicol's prism. Since the two prisms act in a contrary sense, so that the ray which is ordinary in the first becomes extraordinary in the second, there are obtained, if the Nicol's prism situated above the ocular be made to cross that which lies below the quartz, a few black striæ, where equal thicknesses of the latter lie over one another, whilst on both sides colours appear in the sequence of the Newtonian system of rings for reflected light. The prisms, moreover, by sliding can be so arranged that the black stria which is present when the differences of velocity of the rays = 0, or the colour corresponding to some determinate difference of the ray, can be made to occupy the middle of the field.

I now make the upper of the two quartz crystals an object stage, and distribute the muscular fibres of Hydrophilus piceus upon it in such a mode that, whilst some lie parallel to the principal axis, others are arranged perpendicularly to it. If the micrometer screw is now turned so that an increasingly thick portion of the lower prism is gradually brought into the field, it will be remarked that each colour is first assumed by those muscular fibres which are arranged at right angles to the axis of the upper prism, then by the ground, and lastly by the muscular fibres which lie parallel to the axis of the upper prism. If the screw be turned in the opposite direction, these colours are first shown by those muscular fibres which lie parallel to the axis of the upper prism, then by the ground, and then by the fibres which stand perpendicularly to the axis of the upper prism. Every muscular fibre therefore acts optically like a thickening of the prism to the axis of which it is parallel, or, which is the same thing, as an attenuation of the

prism to the axis of which it is perpendicular. The sarcous elements are consequently positive like rock crystal.

The proof of this is obvious. Since the light passes through the first prism at right angles to its principal axis, the plane of vibration of the extraordinary ray is perpendicular to the principal axis, that of the ordinary ray parallel to the principal axis, or at an azimuth of 90° from the former. The extraordinary ray precedes the ordinary, and interference phenomena exhibit differences of shade, which are dependent on the thickness of the prism, and the wave-lengths of the ordinary and extraordinary ray. The two rays emerge from the first prism with this difference of shade, and as they penetrate into the second, which crosses the first at 90°, the ordinary ray can only produce vibrations parallel to the axis, the extraordinary only those which are at right angles to the principal section. Thus the vibrations which constitute the ordinary rays of the first prism form the extraordinary in the second, and *vice versa*. Since now in the second prism the extraordinary ray is propagated with as much increase of rapidity as in the first, it is clear that the difference of velocity must diminish until equal thicknesses of the two prisms are traversed; that it is then = 0; and if the passage through the second prism is longer than through the first, it increases with opposite signs.

If now a doubly refracting body be placed on the upper prism, the optic axis of which is parallel with the principal axis of the crystal, the ordinary ray of this upper prism will be propagated as an ordinary ray in it; and the extraordinary as an extraordinary ray. It acts thus upon the difference of shade as a thickening, if the ordinary in it, as in the prism itself, is propagated less rapidly than the extraordinary; but if the opposite occur, it must operate in the same manner as a thinning of the prism with the principal axis of which its optic axis is parallel.

An important question still remains, which can be solved by the help of the polarising microscope: Are the sarcous elements to be regarded as single and individual elementary bodies, or as groups of solid bodies capable of being variously disposed? If the muscles contract, the fibres are seen to

become thicker, and the transverse striæ to approximate. Each sarcous element must consequently change its form, and become shorter and thicker. If such a change of form result from any force acting in an elementary solid body, the operation of that force must extend as far as the individual molecules, the optic constants must be changed, and it is not conceivable that they should be so changed that the ordinary and extraordinary ray, after they have traversed equal thicknesses in the same direction, should present again the same difference in velocity that they offered under similar circumstances before the change of form.

But it is quite a different matter if the sarcous elements are groups of solid doubly refracting bodies, of which each individual remains unchanged in form in the act of contraction. The form of the whole group—that is, of the sarcous element—is here changed by an alteration in the arrangement of the several corpuscles, just as in a company of soldiers groups of various breadths and depths are produced by changes in the position of the several individuals. In the latter case the optic constants are not altered in the act of contraction, and the rays on this account, if they have traversed equal thicknesses in the same direction, must constantly exhibit the same differences in velocity, whether the muscle be in the relaxed or in the contracted condition.

Since we have a measure of the difference of velocity in the colours which appear under the polarising microscope, we are enabled to answer the question experimentally, whether the optic constants of the contractile substance change during contraction to any considerable extent or not. All the investigations I have directed to this point have had a negative result; *i.e.*, I have never seen any alteration of colour that could not be entirely referred either to changes in the thickness of the layer traversed, or in the angle which the rays undergoing interference make with the optic axis. As, therefore, I have in vain sought after a change of the optic constants, I must maintain that the sarcous elements are not elementary and simple solid bodies, but groups of smaller doubly refractile bodies. These doubly refracting bodies I have called Disdiaclasts, after the phrase employed by Erasmus Bartholin, the

discoverer of double refraction in calc spar, in the title to his well-known treatise.* The composite nature of the sarcous elements furnishes an explanation of the various appearances presented by muscles in a state of rigor mortis. In my researches on the structure of muscular fibres with polarised light,† I have constructed nine different schemes, and we may not unfrequently see one and the same muscular fibre in different parts representing two different schemata, which is attributable to the circumstance that, in the several sections of the fibre, the sarcous elements have divided with great regularity into smaller groups of disdiaclasts, so that much narrower systems of transverse striæ appear in these sections than in others, though they are neither shortened nor thickened by contraction.

Margo,‡ who found that the sarcous elements exist also in the fibres of the adductor muscle of bivalves, frequently saw the muscles in Anodonta only partially striated.§ In this case the sarcous elements of the transversely striated parts lie next one another in regular rows; but in those parts that, with weak powers, appeared homogeneous, he found, with higher powers, instead of numerous small irregularly distributed granules, small groups of disdiaclasts.

If the living muscular fibres of frogs or beetles be immersed in water, they, as is well known, die rapidly; the ends swell up strongly, and the contractile contents ooze out of the sarcolemma. If such terminal portions of fibres be observed under the polarising microscope, with the prisms crossed, no sarcous elements are observed in them, but they present the appearance of fine silvery-grey clouds distributed in the dark

* *Experimenta Crystalli Islandici Disdiaclastia quibus mira et insolita Refractio detegitur.* Havn, 1869.

† *Denkschriften der Wiener Akademie der Wissenschaften,* Band xv., *Separatauflage Wien. bei Gerold.*

‡ *Uber der Muskelfasern der Mollusken, Sitzungsberichte der Wiener Akademie,* Band xxxix., s. 566.

§ The fibres of the adductor muscle were originally erroneously regarded as smooth muscular fibres; that is to say, the substance of which is doubly refracting, but in which neither sarcous elements nor isotropal intervening substance can be distinguished.

field. Here the sarcous elements have become disturbed, whilst the absorbed water has shifted the several disdiaclasts from their position. This state, resulting from the imbibition of water, is essentially different from that induced by the action of dilute acids, which effect a change in the substance of the disdiaclasts themselves, and take away their power of doubly refracting light. In conclusion, I will add a few remarks on the external and internal aids to the study of muscular fibres in polarised light.

To whomsoever the foregoing details and the ordinary works on physical science are insufficient, Aug. Beer's Introduction to the Higher Optics* will prove of service. In the choice of an instrument it is in the next place to be noted that the upper Nicol's prism should be placed over the ocular, and not between the objective (in the more restricted sense of the word) and the so-called collective. Amongst instruments constructed with the latter arrangement I have found nothing better adapted than this for minute and difficult investigation. Böttger, of Berlin, originally furnished the best Nicol's prisms for these purposes; more recently, however, Hartnack, in Paris, has constructed an admirably perfect instrument, arranged according to a method described by him and Prazmowski in the "Annales de Chémie et de Physique," 4e série, T. vii.

The microscopic image can be rendered still more beautiful by distributing the muscular fibres upon a plate of gypsum or mica, attached to the stage by means of Canada balsam, Dammar resin, or Jeffrey's solution of mastic and caoutchouc in chloroform. By appropriate inclination of the gypsum or mica plate a coloured field is obtained, from which the muscles are projected, tinted with different colours, varying in proportion as their inclination on the plate increases or diminishes the difference of the paths which the rays respectively pursue. This experiment has the additional advantage, that the isotropal portions do not entirely vanish as in the dark field, but remain apparent, tinted with the colour of the ground. The most beautiful effects are obtained when the thickness of the little plate is so proportioned that when the prisms are parallel to

* Brunswick, 1853, 800.

one another or crossed, it presents a beautiful purple colour; the muscular fibres then appear blue or yellow, according to their inclination. Amongst the different purple tints which can be obtained, that is the best which first appears in increasing divergence of the rays with crossed prisms, and which corresponds to the purple which is exhibited by Newton's colour glass in reflected light at the limit between the first and the second system of rings. It furnishes in particular the most sensitive field; that is to say, small differences in the divergence of the rays occasioned by doubly refracting bodies lying upon the plate are rendered manifest by relatively great changes of colour. From preliminary investigation with the polarising microscope it is easy to discover, out of a series of gypsum or mica plates of various thickness, those that are best adapted for this purpose, attention being paid not only to the colours themselves, but to the amount of change of colour occasioned by small accidental variations in the thickness of the sections. If the little plates which are used for preserving the preparation contain air between their lamellæ, which collects into bubbles in the preliminary immersion in oil of turpentine, this can be expelled by boiling in turpentine, and allowing it to remain in it till cold. It may then be transferred to the balsam or varnish, with which it and the muscular fibres lying upon it are to be enclosed.

CHAPTER VII.

THE HEART.

By F. SCHWEIGGER-SEIDEL.

THE muscular tissue of the heart presents certain peculiarities which connect it with the structure of those muscles that are subject to the will, whilst, on the other hand, in certain not unessential points it presents characters that are perfectly unique.

The structure is apparently fibrous, although the slightest examination shows that it is impossible to exhibit fibres corre-

Fig. 39.

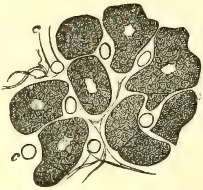


Fig. 39. Small portion of a transverse section through the muscular tissue of the heart. *c*, capillaries.

sponding to the elements of the ordinary muscles. When it is broken up, we for the most part obtain only portions of thin fibrous-like structure, because the fine muscular fibres, dividing frequently and anastomosing with one another, form a close and continuous network.* The contractile substance is transversely

* The anastomosing muscular fibres of the heart, which had already been depicted by Leeuwenhoek, were rediscovered by Kölliker. See his *Mikroskopische Anatomie*, Band ii., pp. 209 and 483. Remak also described the peculiar characters of the muscular tissue of the heart in Müller's *Archiv* for 1850.

striated, sometimes contains fat drops even when apparently healthy, and presents nuclei that are arranged at tolerably regular distances from one another. In the several round or oval disks which are found in sections perpendicular to the direction of the fibres, the nucleus is always in the centre,* excepting in those cases where, on account of the thinness of the section, disks without nuclei happen to be exhibited (fig. 39). The more or less wide fusiform spaces of the contractile substance in which the nuclei lie are filled in the larger specimens with a granular mass, which sometimes (in man) is of a yellow colour (fig. 40, A).

Fig. 40.

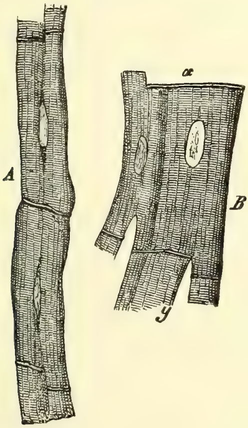


Fig. 40, A. Muscular fibres from the heart of Man, divided by transverse septa into separate nucleated portions. From a preparation preserved in alcohol after having been macerated in a 1 per cent. solution of potash, and in glycerine.

B. Two laterally adherent muscle cells from the Guinea-pig. From a specimen that had been treated with acetic acid and solution of common salt.

The interpretation of the nature of the so-called muscular fibres of the heart is different from that applicable to those of the vo-

* Donder's *Physiologie des Menschen,* 1859, p. 23.

luntary muscles. Weismann* first established, from extended researches in comparative anatomy, that the relations in question are not the same for all the Vertebrata. In Lizards, Amphibia, and Fishes he found the several segments of the cardiac musculature to be formed of closely approximated elongated and fusiform cells, the substance of which presented transverse striæ (fig. 43). In Mammals, Birds, and Reptiles, on the other hand, although an analogous cellular structure could be demonstrated during the embryonic period, yet the anastomosing fibres of the heart must always, he thought, be regarded as formed from the coalescence of isolated cells. Kölliker and Aeby† opposed this view, and the latter observer even found the muscular fibres of adults to be divided into separate portions by transverse septa. But Eberth‡ has recently made an important step in advance, by showing that in two of the above-named groups of Vertebrata a separation of the several cells from one another occurs in the fully developed condition of the muscular tissue of the heart; so that what was commonly regarded as a single fibre turns out to be a complex structure composed of one or many nucleated transversely striated muscle cells.§ Here, therefore, in opposition to the term fibres, applied to the structural elements of the ordinary muscles of the trunk, we may speak of chains of muscle cells or muscle-cell trabeculæ. The difference above referred to between the several groups of animals amounts only to a dissimilar mode of arrangement of the muscle cells, the independency of which in the heart still remains certain. As a proof of this statement, it happens that especially in Mammals we are able to render the limits of the several cells apparent, and to obtain these in an isolated state. The best means for

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* *Archiv für Anatomie und Physiologie*, 1861, p. 42.

† *Zeitschrift für rationelle Medicin*, 3 R., Band xvii., p. 195.

‡ Virchow's *Archiv*, Band xxxvii., p. 100.

§ As long as a division of the cells from one another can be generally demonstrated we can obtain no correct estimate of the degree of coalescence that has taken place; hence it is not easy to discover the difference that exists between the statements made by Kölliker in the fifth edition of his *Handbuch der Gewebelehre*, and those advanced by Eberth. Kölliker now admits that the coalescence of the cells is somewhat less intimate than he had stated it to be.

this purpose is the nitrate of silver, with subsequent application of caustic potass, by the employment of which Eberth was able to split up the muscular substance of the heart into separate prismatic portions, corresponding with the black lines that come into view after treatment with silver, and result from the staining of the connecting substance between the cellular elements. But we may also convince ourselves that, by the application of other means which render the tissue transparent, the muscular fibres are separated into distinct portions by highly refractive transverse lines, and that each of these divisions contains a nucleus. The want of transparency of the contractile substance usually prevents the delicate boundary lines of the cells from being discerned. But in all experiments in which isolation of the fibres is effected it is possible to obtain small nucleated portions of muscle, presenting similar appearances to those seen in fig. 40, B, the single septal line *a* being easily distinguishable from a fissure (*y*) produced by the previous manipulation.

The limiting surfaces of the several muscle cells are not plane. The transverse lines crossing the bundle frequently appear like a flight of steps. Eberth found the borders of the cells more or less regularly dentated. I have, however, observed them to be smooth, and believe the difference to be occasioned by the circumstance that the muscle substance sometimes comes under observation in the contracted, coagulated condition, as after treatment with nitrate of silver, and sometimes in the swollen, distended condition, as after treatment with acetic acid. Other irregularities of form appear to be due to the pressure which the muscle cells exercise upon one another. Every muscle cell contains a nucleus, occupying a central position, or two or more rarely several nuclei may be found, which sometimes lie in close relation to one another, and are of smaller size, thus appearing to proceed from the division of a single one. If the nuclei be widely separated from one another, the question arises, which it is not necessary here to consider, whether the several nucleated cells represent stages of development, or whether there is a disappearance of the cell wall, or, in other words, that it has become incapable of recognition. In adults the solitary nuclei

have a length of about 0·014, and a breadth of about 0·007 millimeters; whilst the muscle cells themselves measure, on the average, 0·050 to 0·070 millimeters in length, and 0·015 to 0·023 millimeters in breadth. The cellular elements are, for the most part, united to one another in the longitudinal direction, but in various parts they send off short lateral processes, which coalesce with those of neighbouring cells, and in this way form the anastomoses that occur between the longitudinal fibres. The cells are only placed in direct apposition to one another, in a transverse direction, in those parts where the stronger muscular

Fig. 41.

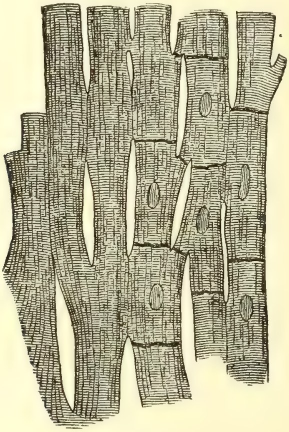

Fig. 41. Anastomosing muscular fibre of the heart, seen in a longitudinal section. On the right, the limits of the separate cells with their nuclei are exhibited somewhat diagrammatically.

trabeculæ are formed. If, however, we consider the abundance of capillaries which, together with nerves and connective tissue, traverse the muscle substance in Mammals, we shall arrive at the conviction that it is impossible for any material to be of a more compact nature. Sections in various directions establish this most satisfactorily, and transverse sections, made from well-hardened hearts (fig. 39), are admirably adapted for the purpose. But in fine longitudinal sections, numerous larger or smaller fissures, arranged in a stellate manner, may also be seen, and so fine that they have been described by some observers as fissures or

spaces within the muscular fibres.* Varying conditions of contraction of the musculature naturally produce variations in the appearances presented. The fissures between the muscle cells are filled, not only by the capillaries, but by a very delicate connective tissue, which, in the form of a perimysium, constitutes sheath-like investments, and appears to consist of isolated branched cells. I have not been able to discover a proper sarcolemma, *i.e.*, a special delicate investing membrane capable of isolation, around the muscle cells, and therefore, in common with other observers, wholly deny the existence of such a membrane investing the muscular fibres of the heart, or, at least, maintain that, if present, it can be demonstrated only with the greatest difficulty.† Nevertheless the cells of muscle, like all other naked cells, must possess a peripherical investment. Independently of the above-mentioned elementary division into fibre cells, the muscular tissue of the heart splits up into coarse subdivisions. By means of septa proceeding from the perimysium, thick fasciculi or bundles are sometimes formed, which, as the well-known columnæ carneæ, are particularly well marked in the auricles. In the walls of the ventricles, on the other hand, the arrangement is rather of a lamellar character, several thin expansions of muscle being so applied to each other as to form a thicker plate, which is visible even to the naked eye.‡ The thinner lamellæ are either connected with one another by extremely delicate connective tissue, or there exists between them certain smooth-edged

* Remak, *loc. cit.*, *Rindfleisch Lehrbuch der Pathologischen Gewebelehre*, 1866, p. 73. Eberth, in accordance with this view, represents longitudinal fissures as existing in the muscle cells; but it may be seen in his fig. 13, that these really indicate the line of union of two adjacent cells. Moreover, Eberth does not appear to attribute sufficient importance to my view of the natural fissuring of the muscle; at least, at p. 121, he observes that the muscular network of the mammalian heart does not exist to the extent attributed to it; but that the appearances seen may frequently be produced by manipulation.

† As to Winkler, who maintains the presence of a sarcolemma in the *Archiv für Anatomie und Physiologie* for 1867, it is obvious from his account of the appearances presented on transverse section, that he really treats of the sheaths of the perimysium.

‡ See Henle, *Handbuch der Systematische Anatomie*, Band iii., Abth. 1; *Gefässelehre*, p. 54, figs. 40 and 44.

fissures, which may be followed for some distance, both in regard to length and depth. These fissures, to which Henle has drawn attention, are in my opinion deserving of particular notice. I find that they are lined by a very delicate membrane, composed of flat cells, the contour lines of which, after treatment with nitrate of silver, appear in the form of a black pattern. Moreover, it is possible to raise up and isolate this membrane after short maceration, which has confirmed me in the opinion that many observers have considered it to represent the sarcolemma. The fissures, in fact, occur in the connective tissue, as may be seen at their angles, and have in rabbits, where, I think, they can best be seen, a length of from 0·06 to 0.25 millimeters. We shall return, however, to this subject hereafter.

The arrangement of the muscular bands in the wall of the heart—the so-called lamination of the cardiac musculature—cannot be fully treated of in this work, since it possesses no histological interest. The careful investigations of C. Ludwig, Pettigrew, Winkler, and others, have, however, shown how complex these arrangements are; and, according to Henle, in addition to all these there must still be added the varieties due to individual differences. The results of accurate examination seem to show that the musculature of the auricles, speaking generally, is divisible into two layers, arranged at right angles to each other, of which the external is circular, but in the case of the ventricles the arrangement of the fibres cannot be described in so simple a manner. We must probably seek for the immediate cause of the spiral arrangement of the muscular bands that here exist in the history of its development, as it is well known that at an early period the cardiac tube forms not only a loop, but a spiral curve, through which necessarily a deviation in the course of both the longitudinal and transverse fibres will be occasioned. Sections made through the wall of the ventricle, in a direction perpendicular to the surface and parallel to the longitudinal axis, exhibit, both externally and internally, longitudinally running bands, whilst the median portion presents transverse sections of the fibres; consequently we can here, though only quite generally, distinguish the two chief directions they pursue.

The connective tissue is closely connected with the muscular substance of the heart, and presents at some spots a remarkable condensation; it is arranged in well-marked layers—this is particularly the case in the so-called fibrous rings at the cardiac orifices, and in a lesser degree at the apices of the papillary muscles, both being points which constitute the origin, or perhaps the termination, of muscular fasciculi. The fibrous rings are composed of very strong fibrous tissue, traversed by exceedingly fine elastic fibres, and sometimes assume to some extent the character of cartilage, the appearances presented resembling those found in true cartilage, at its point of transition into perichondrium. To these differences, which are by no means essential, the somewhat discordant statements and descriptions made by various authors may be ascribed. At the cardiac orifices the fibrous tissue enters into the formation of the valves, and in the papillary muscles it passes immediately into the tissue of the chordæ tendineæ, though always sharply separated from the tissue of the endocardium.

The endocardium forms a membranous lining to the cavities of the heart, but is not everywhere of equal thickness. It participates in the construction of the valves, and is composed of several layers. Its proper basis is formed of an elastic layer, which contains networks of elastic fibres developed to a variable extent, with a corresponding variation in the quantity of connective tissue. The external layer is the loosest in texture. Its internal surface is lined by a layer of nucleated polygonal cells, resting upon a peculiar close-textured lamella of elastic fibres, which constitutes the endothelium of the cardiac cavities.

It may be added that the simple elastic lamina usually adheres closely to the muscular wall itself by means of a layer of connective tissue, whilst the muscular tissue aids in the formation of the endocardium by giving off to it both smooth and transversely striated fibres.

The smooth muscle cells are introduced between the elastic lamellæ, but do not form a continuous layer, being arranged in separate bands, which vary in size, and sometimes attain a thickness of 0·10 millimeters. The several layers of the muscle cells in these fasciculi do not all pursue the same direction, though they generally appear to be divided transversely when the section

has been made perpendicularly to the axis of the heart. These statements are true at least in regard to the endocardium of the septum ventriculorum of man, in which smooth muscular tissue is very distinctly visible.* Moreover, the more externally situated transversely striated muscular tissue of the endocardium does not form a continuous or uniform layer, on which account it may easily be overlooked, or may be regarded as belonging to the muscular layers in general. That the latter is not the case, however, is obvious from the circumstance that the muscular elements in part possess special peculiarities, and also that the endocardial layer is separated from the general musculature of the heart by connective tissue, lymph vessels, and networks of nerves.

Moreover, we find in the endocardium *per se* all the usual layers entering into the composition of the vascular walls, and may therefore very correctly, with Luschka,† identify the endocardium with the whole vessel, and not simply with its tunica intima. It remains to be remarked that the above statements are not applicable to the auricles, since their endocardium, although it possesses considerable thickness, and is remarkably rich in elastic tissue, does not present any proper muscular layers, though here and there a few smooth muscle cells are discoverable.

The transversely striated muscle of the endocardium of the ventricle occurs in two forms, either as the well-known Purkinje's fibres, or as a wide-meshed network of muscular bundles, the elements of which are distinguished from those of the heart by their proportionate size, being broader and shorter. As regards the grey gelatinous-like fibres recognisable by the naked eye, which Purkinje described in 1845 as being situated under the endocardium of the calf, they must partly be considered as a peculiar motor apparatus, and partly as an embryonic form of the muscular tissue

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* Kölliker denies positively the presence of smooth muscular tissue in the endocardium (*Mikroskopische Anatomie*, Band ii., p. 493). Nevertheless, in regard to the localities referred to, no doubt can exist of the correctness of my statement.

† Virchow's *Archiv*, Band iv., p. 171; and *Anatomie*, Band i., Abth. 2, p. 380.

of the heart.* The fibres are united to one another in the form of networks, and are composed of more or less prismatic segments (granules), having a diameter of from 0·05 to 0·10 millimeters, each of which consists of a cortical layer of transversely striated fibrillar muscle substance, and a hyaline axile material containing one or two clear nuclei. Some observers regard the transversely striated mass as an intermediate substance, within which are deposited transparent isolated cells; whilst others, with whom I agree, regard each granule as a muscle cell, in which (as in a certain stage of development) only the peripheric layers have undergone conversion into contractile substance.

In what relations these segments of the fibres of Purkinje stand to the cardiac muscle in its fully developed condition, is a subject that can only be elucidated by a knowledge of the history of development; but it may here be remarked that various observations have been made, which agree in showing that the fibres of Purkinje pass directly into ordinary muscular bands, and that in some animals their place can be supplied by ordinary muscular tissue. The controversy whether this or that animal possesses the fibres of Purkinje is therefore of small importance, because the differences depend merely upon the various forms presented by the endocardial muscle.

A division of the stronger fibres, as we have already seen, does not occur here, whilst they are for the most part surrounded by a well-marked sheath of connective tissue. These sheaths, when penetrated by an injection pipe, sometimes become filled with injection, and then form a wide-meshed network which it is impossible to mistake for the vessels of the lymphatic system (Eberth).

As already indicated in discussing the internal membrane of the heart, we have to consider the *valves*. These indeed are usually considered to be duplicatures of the endocardium, but this expression is not absolutely correct. The substance

* Besides the work of Purkinje (Müller's *Archiv*, 1845, p. 294), reference may be made to the statements of Kölliker, Hessling, Reichert, Remak, Aeby, Obermaier, and Lehnert. More exact and extended references to the literature of the subject will be found in the last-named authors. Obermaier, *Archiv für Anatomie u. Physiologie*, 1867, pp. 245 u. 358; Lehnert, Max Schultze's *Archiv für Mikroskopische Anatomie*, 1868, p. 26.

of these valves consists essentially of two lamellæ, a fibrous and an elastic; the former is directly continuous with the fibrous rings, the latter in the case of the venous valves is a prolongation of the endocardium of the auricle, but in the arterial valves it is a prolongation of the membrane lining the ventricular chambers. The free surface of the fibrous layer is invested by a thin membrane composed of cells which do not rest upon any special elastic substratum, except that perhaps the elastic element of the fibrous layer itself undergoes a slight thickening at the margin. In the semi-lunar valves the elastic layer is considerably thickened, whilst at the attached border of the venous valves the two layers disappear towards their apices, their place being supplied by the tolerably abundantly nucleated tendinous tissue of the chordæ tendineæ. The latter near the musculi papillares possess an external elastic layer with a delicate investing membrane composed of cells, which constitutes a prolongation of the endocardium.* At the apices of the valves muscular bundles pass directly into the endocardium of the auricle, and extend to a greater or less distance downwards, but in all instances are limited to the upper portion.†

According to the statements of Oehl,‡ small isolated muscles are present in the larger tendinous cords of the left auriculo-ventricular valves. The fibres of Purkinje are continuous with the chordæ tendineæ. Villous processes or outgrowths are sometimes found attached to the valves (Luschka, Lambl.). In regard to the endocardium in general, it should be mentioned that the microscopic appearances which are found in various animals differ chiefly in the greater or less development of the elastic network of fibres. The foregoing description is chiefly taken from observations made on the heart of man.

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* Analogous observations were formerly made by Donders, in regard to the structure of the valves. I cannot agree with the statement of Luschka, that the valves are the direct continuation of the arterial wall, *Archiv für Physiologische Heilkunde*, 1856, p. 537; compare also Henle.

† Amongst the most recent investigations on the musculature of the auriculo-ventricular valves are to be enumerated those of Gussenbauer, *Sitzungsberichte der Wiener Akademie der Wissenschaften*, Band lvii., Abth. 1.

‡ *Mém. d. Acad. d. Scienze d. Torino*, Vol. xx., 1861.

The *pericardium*, in opposition to the endocardium, is a serous membrane, and possesses the general characteristic peculiarities of such membranes. The subserous tissue is occasionally marked by the presence of a large number of fat cells.

The *bloodvessels* are branches of the coronary arteries, and are distributed in the muscular substance, as well as to the pericardium and endocardium. The vessels of the last-named membrane extend, according to Luschka, into the valves. The capillary vessels distributed through the muscular substance of the heart are very numerous, the muscle cells themselves being enclosed in a network of vessels. The rootlets of the veins are formed by several capillary vessels uniting directly to form a thicker trunk; an arrangement by which, we may conclude, the discharge of the blood is facilitated.

In reference to the *lymphatics* of the heart, we possess recent investigations by Eberth and Belajeff;* and, as they have pointed out, a network of lymph capillaries of the ordinary kind may be distinguished both in the pericardium as well as in the endocardium, the meshes of which are sometimes large and sometimes small, and are usually arranged in a single layer, but occasionally, where the thickness of the membrane is considerable, in several layers. The endocardial lymphatic network of the auricle is continued by means of a few finer tubes upon the auriculo-ventricular valves, and reaches nearly to their middle. In the same way a few lymph tubes may be traced as prolongations of the network of the endocardium of the ventricle into the semi-lunar valves. In the muscular substance of the heart itself the above-named observers found, in opposition to Luschka, that the lymph vessels were "not so numerous," whilst I conclude, from my own researches, that the muscular substance of the heart stands in still closer relation to the lymphatics than appears from their statement, because I am of opinion that the formerly described fissures of Henle found in the muscular substance must be regarded as a portion and continuation of the lymphatic system. But since these fissures are connected at many points with one another, they form a canal system, permeating the muscular substance to an extent which certainly cannot be termed sparing.

* Virchow's *Archiv*, Band xxxvii., p. 124.

It has already been mentioned that the smooth fissures are covered with a delicate membrane analogous to the endothelium of the lymphatics, to which it must also be added, that it is easy to follow sub-pericardial lymph vessels and their prolongations into the lacunar system. That this system cannot be injected through the vessels constitutes no objection to our view, On sticking an injection pipe into the muscular substance of the heart, the fluid penetrates between the several elements of the muscles into the perimysium, and may become widely diffused, so that with slight pressure we may even see the injection penetrating into the lymph vessels of the pericardium without any evident rupture or extravasation. A complete injection of the lacunæ cannot be obtained in this manner. It is observable that the lymphatics of the muscular substance are not always in the form of fissures, but sometimes assume a tubular form, dependent upon the amount of injection forced in, and upon the degree of contraction of the muscular substance.

In regard to the finer distribution of the *cardiac nerves*, which is of peculiar physiological importance, little is at present known, and our knowledge is particularly defective in reference to the more intimate histological relations of the fibres springing from various sources and distributed to the different tissues.

The nerve fibres proceeding from the plexus cardiacus lie in mammals beneath the pericardium, but in part also they are found in the septum ventriculorum, where they run in the substance of the muscular mass and in the spaces between the two ventricles. Their distribution under the pericardium is independent of the vessels, and it even appears in some animals that the nerves cross the superficial muscular fasciculi and the vessels at right angles, as is clearly shown in the illustrations given by Lee.*

The isolated, somewhat flattened fibres, which intercommunicate by means of delicate fasciculi, consist chiefly of non-medullated nerve fibres. The double-contoured fibres vary in relative proportion, but are usually only sparingly present. The nerves

* R. Lee, *Philosophical Transactions*, London, 1849, Plates ii. and iii.

enter into communication with ganglion cells. These, united into groups, lie on the external surface of the fasciculi of fibres, and sometimes form small detached ganglia, which are connected with the nerve by a peduncle. Accumulations of cells of materially larger size do not occur, whilst in particular the enlargements of the nerves perceptible to the eye are occasioned simply by the penetration into their substance of connective tissue, accompanied by large vessels.

The relation of the fibres to the ganglion cells can be better studied in the cardiac nerves of the frog than in the sub-pericardial nerves of mammals, as the former spread out in the thin interauricular septum, and are very well known in regard to their course of distribution, in consequence of several special works having been devoted to them (C. Ludwig, Bidder). The greater number of ganglion cells exhibit the structure peculiar to the cells of the sympathetic, in which from one and the same pole, besides the so-called straight fibre, there originates also the spiral fibre of Arnold and Beale, which has elsewhere been fully described. Besides these, however, as has been shown by various observers, true bipolar cells are present, and, lastly, also ganglion cells, characterised by the peculiar mode of their arrangement, which, if we accept the view of Auerbach,* are found "in opposition,"—that is to say, two pear-shaped cells lie in a common sheath with their flat sides applied to one another, whilst the nerve fibres issuing from their pointed extremities course in opposite directions. The approximation of such binary cells being very close, especially when they are examined in the fresh condition, they may easily be mistaken for simple bipolar cells. No spiral fibre is here present.

Auerbach found this form of ganglion cell in the plexus myentericus, Bidder in the auricular septum, and I myself in other sympathetic ganglia. According to my views, those cells from which two straight fibres can be seen to issue, belong to the same category, since as many even as three small ganglion bodies may be found invested by a common capsule.

Since the influence of the nerves on the activity of the heart has been more accurately investigated, the view has generally been ad-

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* Virchow's *Archiv*, Band xxx., p. 458.

mitted that the difference between the vagus and the sympathetic, or, in other words, the difference between the inhibitory and the exciting fibres, is to be sought for in the circumstance that the one acts directly on the muscular substance, the other only indirectly through the intervention of the ganglion cells. The latter is supposed to be the mode in which the vagus acts, though no positive proof of the fact has hitherto been adduced.

Kölliker, indeed, has convinced himself from anatomical investigation that the vagus stands in no direct relation with the ganglion cells, but other observers do not agree with him; and very recently Bidder,* who has also examined the subject anatomically, has stated that the spiral fibres are fibres of the vagus passing to the ganglion cells, whilst the straight fibres are given off by the cells, and are destined to be peripherically distributed. If, however, Bidder rests his view exclusively on the results of sections of the nerves made in frogs, his evidence is diminished in value to some extent, because in these animals the Rami Cardiaci are the only nerves which pass to the heart; and consequently, when they are divided, not only the inhibitory, but the exciting fibres would undergo degeneration.

The further distribution of the nerves in the muscular substance of the heart is difficult to follow, as they undergo rapid subdivision, or, at least, but few trunks can be seen. Hence it follows that the fibres are delicate and non-medullated. It is generally acknowledged that ganglia are distributed in the muscular substance. If, however, this be admitted on the authority of Remak,† it is to be remarked that he observed their presence under the microscope only in the case of the calf. I have not been myself successful in discovering such ganglia lying between the fibres in the proper muscular substance, and can only admit that they may be found on a few traversing trunks or branches.

Friedländer maintains that large numbers of ganglion cells are present in the muscular substance of the heart of the frog, as he believes he has demonstrated the constant existence of such

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* *Archiv für Anatomie u. Physiologie*, 1868, p. 1.

† Müller's *Archiv*, 1844, p. 463.

‡ *Untersuchungen aus der Physiologische Laboratorium in Würzburg*, Heft. ii., 1867.

cells in still pulsating portions of muscle, in which there were not, in some instances, more than two or three muscular fibres. His statements, however, are not sufficiently precise. He has given no description of either the size, form, or appearance of the supposed ganglion cells, and has made no investigations to show their connection with nerve fibres.

We possess a few observations respecting the mode of termination of the nerves in the muscular tissue of the heart, that have been made by Kölliker and Krause. Kölliker considers that in the frog the pale nucleated fibres running on and in the secondary muscular bundles, terminate in the same mode as the nerves of the voluntary muscles; whilst Krause states that "the double-contoured nerve fibres of the cardiac muscle end in motor terminal plates; and hence the peculiar operation of the cardiac nerves receives no explanation from the mode in which they terminate."*

That the relations of the cardiac nerves must differ from those distributed to the muscles of the trunk is probable on *à priori* grounds, from the different arrangement of the muscular elements; for, as the several muscle cells preserve their independence, it is easy to conceive that their mode of innervation would be peculiar, and would present an analogy to that of the smooth muscular tissue. Further inquiry is requisite to determine the precise mode in which the ultimate distribution of the nerves is effected, but the following remarks may be provisionally made for the purposes of comparison with the arrangements presented by other muscles.

The nerves run in the connective tissue accompanying the capillaries and occupying the fissures between the muscle cells, and appear in the form of delicate nucleated fibres, resembling those which are elsewhere seen to constitute the peripheric terminations. It is difficult, even in very thin layers of muscle, to discover the extremely delicate fibres. The nuclei of the capillaries, of the nerves, and of the muscle, however different their characters may be, confuse the microscopic image to so great an extent that no other course

* *Anatomie des Kaninchens.* Leipzig, 1868, p. 178.

is left but to isolate the nerves by dissolving out the network of muscle cells.

If specimens be taken from the middle of the ventricular wall of Mammals, we may obtain, in successful cases, numerous nerve fibres, though usually only in fragments, and may see how frequently they divide, and, with great clearness, the mode in which they form networks (fig. 42). The divisions are, in some

Fig. 42.

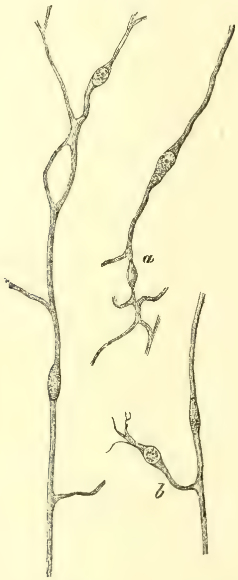

Fig. 42. Isolated nerve fibres from the muscular substance of the wall of the ventricle. From the Dog. Magnified 500 diameters.

parts, very numerous (a), though the lateral branches are for the most part torn off. We seldom meet with such a case as is represented at b, and when seen, there must always remain a doubt whether a natural termination is under observation, because the fibrils issuing from the second nuclear swelling are so fine that no sure ground is afforded to determine whether or no they are broken off. In the Frog, the arrangement is so far different that no capillaries exist in the muscular mass, and

the individual bundles are composed of closely compressed fusiform cells. In fig. 43, two trabeculæ are exhibited from the auricle, partially detached from each other. Fine nerve fibres, with the ordinary nuclei, intervene between them, and, after frequently undergoing subdivision, become closely applied to the muscular fasciculi. (The branch *a* runs beneath the

Fig. 43.

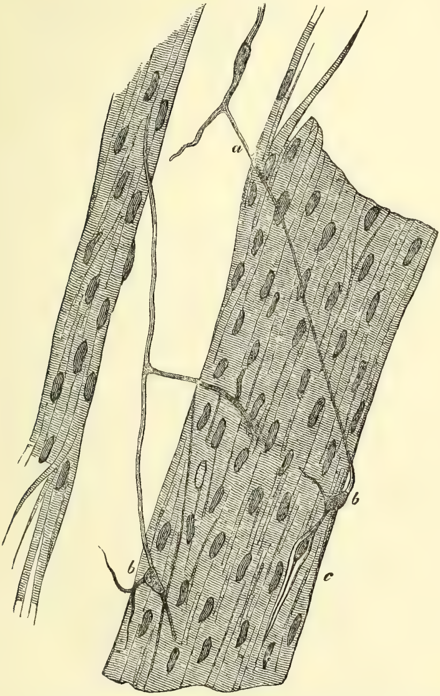

Fig. 43. Trabeculæ of muscle from the auricle of the Frog, with the nerves.

fasciculus.) Fine fibres are, as usual, given off from the characteristic triangular nuclei, which penetrate into the interior of the fasciculus, and it may then easily be seen that the nucleated fibre *c* lies in a space between the muscle cells. By carefully isolating the tissues, very fine branched fibrils may

be exhibited, which might be regarded as nervous in their nature, even without any direct connection with undoubted nerve fibres being discoverable. Such fine fibrils sometimes adhere firmly to the muscle cells.

Notwithstanding the doubts that exist on some of these points, it may be regarded as well ascertained that the finer branches of the cardiac nerves lie between the proper elements of the muscle, and so come into immediate contact with the contractile substance which is here destitute of sarcolemma. As to what proportion the number of terminal nerve branches bear to the number of muscle elements, no positive statement can at present be made. I have not been able to observe any such direct connection between the nerves and the nuclei of the muscle cells as has been stated by Frankenhäuser in regard to the smooth muscles.*

It still remains to notice other parts in which ramifications of the cardiac nerves occur, and of these the first that may be mentioned is the pericardium, in which, as in other serous membranes, networks of fine fibres are present. And, secondly, the endocardium, in which a very considerable development of nervous tissue exists. This distribution is not exclusively connected with the presence of muscular layers, since, besides motor, we must certainly admit the existence of other nerves with different endowments. The latter terminate in the inner laminæ of the membrane; but their finer branches, in consequence of the elastic tissue present, are only to be discovered with difficulty, and require the application of chloride of gold.† They are nucleated, and form networks in the membrane which are analogous to those ordinarily found in serous membranes, except that the meshes are much narrower. Since, however, there is no regularity in their distribution, any attempt at comparative measurement would only be applicable to special

* To enter more minutely on this subject, and to give the details required for making special investigations in it, would lead us too far, and the consideration of these points must therefore be reserved for discussion elsewhere.

† The above statements are based on hitherto unpublished investigations that have recently been made under my direction by Dr. Schmulewitsch.

instances. The nerves terminate in a manner essentially similar to those of serous membranes generally, though it is here extremely difficult to arrive at any positive conclusions.

The plexus of coarser fasciculi lying in the subserous connective tissue, and therefore beneath the muscular layer of the endocardium, and which can easily be brought into view, must be distinguished from the fine networks of fibres above described. Isolated fibres are given off from them, which partly end in the muscles and partly enter into the formation of the abovementioned fine networks.

CHAPTER VIII.

THE BLOODVESSELS.

By C. J. EBERTH,

PROFESSOR OF PATHOLOGICAL ANATOMY IN ZURICH.

In adult vertebrate animals the essential constituent of the bloodvessels is a tubular system formed of a single layer of flat cells, or of a delicate nucleated membrane, termed the endothelial tube by His,* the perithelial tube by Auerbach,† and the cell membrane by Remak.‡ This tube is the least variable part of the vascular walls, and is present alike in the finest bloodvessels, in the largest trunks, and in the dilated portions of the vascular system—the heart and the several sinuses—however much the other constituents of the vascular wall may vary. In a few organs, however, as in the spleen of Mammals, in the pulmonary organs of the Cephalophora, and in the gills of Crustacea, the passages through which the blood courses appear to be destitute of a proper wall.§ The capillaries and smaller veins are formed of this tube alone, the elementary constituents of which are delicate, flattened, more or less fusiform, or polygonal cells, composed of a nucleus with surrounding protoplasm, and arranged for the most part parallel to the long axis of the vessels.

In the heart and arteries, and in most of the veins, this cell tube is invested by connective tissue and by elastic and

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* *Die Häute und Höhlen des Körpers.* Basel, 1866.

† Virchow's *Archiv*, Band xxxiii., 1865.

‡ Müller's *Archiv*, 1850.

§ Bidder, in his *Beiträge zur Gynäkologie und Geburtskunde, v. Holst*, 1867, has incorrectly denied the presence of an endothelium in the marginal veins of the placenta. See Eberth, Virchow's *Archiv*, Band xliii., p. 136, 1868.

muscular elements, which are frequently arranged in layers, but are often also irregularly combined into a tunic, that in opposition to the internal cellular membrane may be called the *external vascular coat* or *investing membrane.* The thickness of this membrane does not increase proportionally to the diameter of the vessel, as there are wide vessels with very thin, and small vessels with comparatively thick coats. Amongst the Invertebrata, as in snails and mussels, even the large lacunar blood spaces which surround the viscera are bounded only by a very delicate cellular membrane, which invests the various organs as an external epithelial tissue, similar to the epithelium of the peritoneum.

The smaller vessels have thicker walls in comparison with the larger, but the several components of the wall do not participate to an equal extent in producing this increase of thickness. It is chiefly effected by an augmentation of the muscular tissue, which becomes abundant in proportion to the diminution in the quantity of the elastic and connective tissue.

The tissues which form the investing tunics are arranged in layers, the thickness of which, as well as the order of their succession, undergo many variations.

The investing layer is limited internally by an elastic membrane termed the *internal elastic coat.* The external surface of this membrane is covered by a muscular layer composed of smooth muscular fibres, which are partly arranged in a circular and partly in a longitudinal direction. This layer is termed the *middle coat* in consequence of the position it occupies between the elastic coat on the one hand, and the *external coat* or *tunica adventitia,* composed chiefly of connective tissue and elastic fibres, on the other.

To these tunics must still be added a fourth connective tissue layer—*the internal tunic* or *internal longitudinal fibre layer,* which lies between the endothelium and the elastic internal coat, and which I shall term the *intermediate layer.* In the arteries it is only present in the larger vessels, and is gradually lost towards the periphery. In the veins it attains its maximum in some of the peripheral vessels, and diminishes towards the heart, so that it is almost entirely absent in such large vessels as the vena cava.

Besides the above-named elements the vascular walls contain elastic fibres and sheets, which sometimes appear as finer or coarser fibres arranged in a retiform manner, at others in the form of strong broad bands, and sometimes as fine striated lamellæ and membranes. The elastic fibres form a network extending through the whole thickness of the investing layer, the proportional development of which varies not only in different portions of the vascular system, but also in the different coats. Such fibrous networks attain a great development in the arteries on the external surface of the muscular tunic, where they often form a strong and tolerably well-defined layer. (Henle's *external elastic coat.*)

Vasa vasorum and Nerves.—The tunica adventitia of the large arteries and veins possesses arteries, capillaries, and veins which may extend even into the external layers of the muscular coat. The inner fibrous membrane is destitute of vessels.

Lymphatics have not hitherto been traced into the coats of the bloodvessels. The lymphatics of the endocardium only extend as far as the semi-lunar valves.*

In Amphibia and Reptiles, the large vessels, and especially the arteries, lie in the interior of immense lymphatic spaces, and are invested by the cell membrane of the lymphatics.

The perivascular spaces in the brain and spinal cord of Mammals, which were formerly regarded by His as lymphatics,† are, according to his more recent investigations, as well as mine, only lacunæ in the tissue, and possess no proper walls.

With the exception of the capillaries, the presence of nerves has been demonstrated in all vessels, even in the tunica adventitia of the non-muscular veins of the pia mater. These, partly consisting of dark-edged and partly of pale fibres, break up after they have traversed the tunica adventitia into a fine network. The fibres of this network, according to my observations on the small cutaneous vessels of the frog, are of the most delicate description, whilst the network is of the closest character.

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* Eberth and Belajeff, Virchow's *Archiv*, Band xxxvi., 1866, p. 124.

† *Zeitschrift für wissenschaftliche Zoologie*, Band xv., 1865, p. 127.

I have not been able to convince myself of the precise mode in which they terminate, especially in regard to the muscles.

Ganglion cells occur in the course of some of the afferent nerve fibres, and in the coarser plexuses. Beale* considers them to be very widely distributed. I have recognised them only in the inferior vena cava of the Frog, where they were first discovered by Lehmann.† Heaps of small, somewhat flattened, and closely compressed ganglion cells unite to form roundish nerve knots.

ARTERIES.

The arteries are distinguished from the veins by their thicker walls, resulting from the greater development of their muscular and elastic fibres. The thickness of the entire wall increases, though not proportionally to the increase of the calibre of the vessel. The thickness of the muscular tissue increases with the diminution of the calibre. The quantity of elastic fibres, on the other hand, increases with the calibre. The *cellular layer* of the arteries consists of fusiform or, occasionally, polygonal cells, which vary but little in diameter in the various vascular provinces.

ELASTIC INNER COAT.—The innermost layer of the external vascular coat—the elastic membrane of Donders, the elastic internal tunic of Kölliker, the elastic longitudinal fibre layer of Remak—consists in the finest vessels of a network of fine elastic fibrils, or of a delicate structureless elastic membrane, which, in collapsed or bent vessels, or when separated from its attachments, exhibits fine parallel, longitudinal, and transverse folds. It can be distinguished even in very fine tubes possessing only isolated muscle cells. Towards the larger vessels the membrane increases in thickness; small rounded or elongated spaces occur in it, and it now appears as a fenestrated membrane thickened with longitudinal rugæ (Arteria basilaris). In the larger vessels the fenestræ are more numerous; the

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* *Philosophical Transactions*, cliii., p. 562.

† *Zeitschrift für wissenschaftliche Zoologie*, Band xiv., p. 346.

membrane, in consequence, assumes the appearance of a network composed of fibres of varying thickness, or of a fenestrated membrane with plexiform thickenings. Large trunks,

Fig. 44.

Fig. 44. Endothelium of the carotid artery of Man, after treatment with nitrate of silver. *a*, cells; *b*, clearer; *c*, darker intermediate spaces; *d*, intra-cellular circular and spotted markings.

such as the axillary, carotid, pulmonary, crural, popliteal, and hepatic arteries, instead of a simple elastic membrane, possess two or three anastomosing lamellæ, or plexuses of elastic tissue, a clear, but slightly fibrous connective tissue filling up their interspaces.

Internal Fibrous Coat.—With the above membrane is associated a second, which, however, is not, as Henle* main-

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* *Allgemeine Anatomie*, p. 496.

tained, situated between it and the next coat, the so-called tunica media; but, according to the observations of Kölliker,* Gimbert,† and myself, occupies a position intermediate between the epithelium and the elastic inner tunic. Remak has designated this layer as the *innermost longitudinal fibrous coat;* Kölliker, as the *striated layer of the internal coat.* This coat consists of a finely granular substance, with delicate fibrils

Fig. 45.

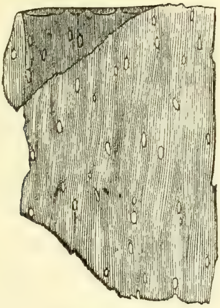

Fig. 45. Elastic internal tunic of the basilar arteries.

running transversely and longitudinally. The greater part of this tunic is destroyed by the action of potash. Externally, this membrane becomes more distinctly fibrous, and gradually passes into elastic networks and membranes.

According to Langhans,‡ this layer is not distinctly fibrous in young persons, but indistinctly granular, the striation first becoming apparent after the membrane has attained a certain thickness.

The tissue of this membrane contains numerous fusiform and stellate cells, lying in anastomosing canals, with relatively large nuclei, and with either finely granular or quite homogeneous cell substance. Amongst these elements small granulation cells are sometimes found, respecting which it is a matter

* *Handbuch der Gewebelehre*, 5. Auflage, p. 583.

† *Mémoire sur la structure et sur la texture des Artères, Journal de l'Anatomie et de la Physiologie*, par Charles Robin, p. 536, 1865.

‡ Virchow's *Archiv*, Band xxxvi., p. 197, 1866.

of doubt whether they are to be regarded as normal or pathological constituents. In some instances, the nuclei of the fusiform cells present so well marked a rod-like form as to lead to the supposition that smooth muscles are present. But, like Kölliker,* who first drew attention to them in the axillary and popliteal arteries, I have been unable to convince myself of the presence of smooth muscles in the internal coat of these vessels. On the other hand, I have met with isolated muscle cells in the internal longitudinal fibrous tunic in the hepatic and splenic arteries, and in the crural, at the points where they divide.

MUSCULAR COAT.—The transition of a capillary into an arterial tube commences with the appearance of scattered transversely disposed fusiform muscle cells, immediately external to the endothelial tube, and between it and the tunica adventitia.

The muscle cells, which at first form only a single interrupted layer, gradually increase in number, and come to constitute an independent layer of cells, adjoining to and superimposed upon each other. Externally, this layer is, for the most part, sharply bounded by the external elastic tunic, or by the tunica adventitia, and internally by the inner elastic membrane.

I find that a short portion of the pulmonary artery and the aorta, immediately above the attachment of the semi-lunar valves, are destitute of muscle.

Many arteries possess no muscles whatever. Leydig † found none in the aorta of Balæna musculus, nor in the aorta and other larger arteries of Raja batis, Spinax niger, and Polypterus, nor in the basilar artery of the brain of Scymnus lichia, the fine cerebral arteries of which, however, contain distinct circularly arranged muscles.

With the exception of the largest arterial trunks, the muscular layers consist of finely granular connective tissue, containing scattered cells, and traversed by a few fine elastic fibrils, in which lie a number of muscle cells, more or less

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* *Zeitschrift für wissenschaftliche Zoologie,* Band i., p. 81, 1849.

† *Lehrbuch,* 1857.

closely packed. In the more peripherically situated vessels the quantity of this intermediate substance diminishes, and the muscle cells are in closer proximity with one another. In the larger arterial trunks, as the aorta, pulmonary, subclavian,

Fig. 46.

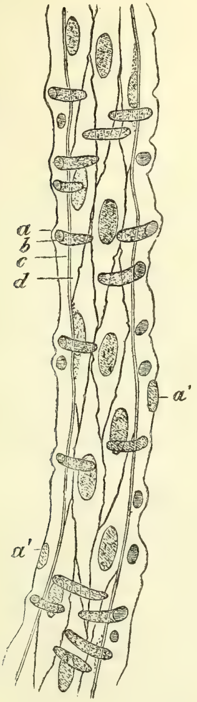

Fig. 46. Small artery from the brain of Man. *a*, tunica adventitia; *a'*, a nucleus of the tunica adventitia; *b*, muscle nucleus; *c*, elastic internal tunic; *d*, cell membrane formed of fusiform cells.

and carotid arteries, the intermediate substance is not only so abundant that the short and isolated muscle cells, and the smaller groups of such cells, are separated from one another by large intervening spaces, but the elastic tissue also attains its greatest development in the muscular layers. Associated with the fine and narrow-meshed elastic-fibre networks which traverse

the fibrous, granular intermediate substance, are a series of lamellæ of tolerably even width, composed of elastic bands and fenestrated membrane. These, arranged at nearly regular intervals, constitute septa, dividing the muscular tunic into numerous layers. The lamellæ are connected by numerous oblique anastomoses, and are also continuous with the fine elastic fibres. They chiefly pursue a transverse direction.

In man, at least, there is always a layer of circularly arranged muscle cells, which, however, are strengthened by oblique or longitudinal muscular fasciculi, that are sometimes situated externally, sometimes internally, to the circular fibre layer, and sometimes occupy both positions.

Scattered longitudinally and obliquely disposed muscle cells are found in the descending thoracic aorta between the transverse muscular fibres. The large vessels that, on account of their loose connections, are easily moved, like those of the viscera of man and mammals, the arteria lienalis, renalis, umbilicalis, and dorsalis penis, are particularly characterised by longitudinal muscular bundles.

The longitudinal muscles of the arteries are chiefly situated in the tunica adventitia, especially in its internal and middle

Fig. 47.

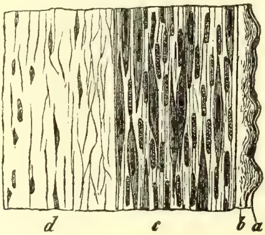

Fig. 47. Transverse section of the coats of the basilar artery. *a*, endothelium; *b*, elastic internal membrane; *c*, muscle cells; *d*, tunica adventitia.

layers, where, however, they seldom form a continuous layer, but are united into fasciculi of greater or less strength (arteria renalis, lienalis, dorsalis penis). A well-developed longitudinal muscular layer invests the circular fibrous layer, which is also strongly marked in the arteries of the mesovarium of Batrachia. The

adventitia of the crural artery contains a few short longitudinal fasciculi. According to Remak,* both in man and various mammals (ox, sheep, pig), small bundles of longitudinal muscles, apparent even to the naked eye as whitish masses, are recognisable on the external surface of the arch and thoracic portion of the aorta.† In oxen, sheep, and pigs, Remak was able to follow the longitudinal muscles as far as the iliac arteries, and in the sheep he found them in the pulmonary artery and its branches. In the arteries distributed to the

Fig. 48.

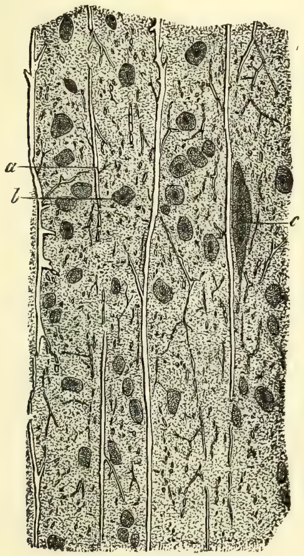

Fig. 48. Longitudinal section through the coat of the thoracic aorta. *a*, elastic plates; *b*, transverse muscles in section; *c*, longitudinal muscles.

viscera, Remak found external longitudinal muscles only in the trunk and in the primary divisions of the superior mesen-

* Müller's *Archiv*, p. 96, 1850.

† I can corroborate this statement in the case of the calf.

teric, the splenic, and renal arteries of oxen, but in the sheep they are scarcely perceptible in the arteria mesenterica. In both, the bundles are collected into a thick uninterrupted longitudinal layer.

I was only able to find internal longitudinal muscles in the form of isolated cells in the internal longitudinal fibrous tunic of the hepatic, splenic, and crural arteries. I was not able to discover them in the remaining abdominal vessels, nor in the axillary and popliteal arteries, where Kölliker believed he had recognised them.

A delicate layer, composed of contractile longitudinal fibres, exists, according to Remak, in the internal longitudinal fibrous tunic of the renal, splenic, hepatic, and mesenteric arteries of man, the ox, sheep, and pig. These muscles, however, are only found near the origins of these vessels, and on the proximal side of the point at which the branches are given off from the trunk. In oxen, these muscles form thick, strongly projecting longitudinal cords that are crossed by strong circular fibres near the larger openings, and there constitute a kind of sphincter.

Through these longitudinal muscles the openings of the less fixed vessels, given off at acute angles, are probably kept contracted when, in consequence of the strong contraction of the discharging vessels, the passage of the blood is checked. This longitudinal fibre layer is absent in those vessels where, on account of their fixity, and the equality of the strength of the blood column, this provision is not required, as in the innominate, carotid, and subclavian arteries.

I have observed scattered longitudinal muscles in the tunica interna, at the points where branches are given off at acute angles, as at the division of the external iliac into the femoral and profunda arteries.

Distinct external and internal longitudinal muscles are only found in the extremely muscular umbilical arteries. The circular muscular layer is here lined internally by a continuous layer of longitudinal muscles, and externally by interrupted and slender muscular bundles, running in the same direction.

External Elastic Coat, and Tunica Adventitia.— The

external elastic tunic of Henle* exists as an independent membrane in the smaller and medium-sized arteries, with few exceptions (internal spermatic, splenic, renal, hepatic, brachial, crural, popliteal and plantar arteries).

The basilar artery, the muscular tissue of which is poor in elastic fibres, loses this membrane completely, and presents instead a very loose network of fine elastic fibres in the tunica adventitia. The dorsal artery of the penis contains similar and numerous elastic networks. The aorta, axillary, carotid, subclavian, and pulmonary arteries, whilst they present largely developed elastic laminæ in the muscular tunic, do not possess a proper external elastic membrane.

Speaking generally, this membrane is formed by a network of fine elastic fibres, which is sharply defined internally towards the muscular layer, but which externally anastomoses with the elastic network of the tunica adventitia. The remaining portion of the adventitia consists of decussating fasciculi of connective tissue, with networks of elastic fibres.

After what has been said, it is obvious that, whilst a description can be given which shall be applicable to individual arteries, and to groups of arteries, no general statement can be given that is appropriate to the entire arterial system; there is, in fact, a certain antagonism between the elastic element of the tunica adventitia and that of the circular muscular layer, as is well shown in the case of the basilar artery. Still more frequently, again, there exists a certain antagonism between the muscles and the elastic elements of the circular muscle layer. If, in any vessel, the muscles preponderate, the elastic fibres diminish and recede towards the adventitia.

The Veins.

Veins differ from arteries in possessing thinner walls, less elastic and muscular tissue, and for the most part a stronger tunica adventitia.

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* *Allgemeine Anatomie*, p. 502; *Handbuch der Anatomie des Menschen*, Band iii., p. 73; *Gewebelehre*, von Kölliker; *Luigi Fasce, Istologia delle arterie e delle vene degli animali vertebrati.* Palermo, 1865.

THE EPITHELIAL LAYER consists of cells that, when compared with the corresponding structures in the arteries, present a more polygonal and less distinctly fusiform shape, and are consequently both shorter and broader. Their size varies in different regions.

ELASTIC INTERNAL MEMBRANE.—The veins, like the arteries, possess an elastic membrane, situated immediately beneath the epithelium, and apparent even in small vessels. This tunic never acquires the size and strength it exhibits in the arteries, and usually appears as a delicate and rather loose network of fibres, which, for the most part, run in a longitudinal direction, and but rarely, as in the larger trunks, undergo development into a fenestrated elastic tunic. In the iliac and crural veins this coat appears in some places to be split into two laminæ, which intercommunicate with one another by fine elastic fibrils. A delicate indistinctly fibrous connective tissue containing longitudinally and transversely arranged short fusiform cells, occupies the interspaces of this network.

The internal longitudinal fibrous tunic is situated between the epithelial layer and the internal elastic membrane, as in the arteries, but is developed to a much less extent. In some veins it is almost wholly absent, as in those of the neck, the axillary vein, the vena cava, the mesenteric and portal veins, the vena azygos, and the branches of the pulmonary vein. The thickness of this layer by no means corresponds with the size of the vessel. Thus it is absent in the vena cava inferior, both above and below the liver, reappearing in the iliac vein, and increasing gradually in strength until the popliteal is reached, where it attains its greatest thickness. At this part the membrane often forms thickenings, which appear even to the naked eye as small elevations and transverse rugæ. On tracing it further towards the periphery its thickness will be found to undergo gradual diminution.

Its structure is essentially similar to that of the same layer in the arteries, with the exception that in many parts numerous muscles are present which fail to appear in the corresponding arteries. Thus the crural vein presents small bundles of longitudinal muscular fibres between the laminæ of its elastic inner coat, and the popliteal possesses in the same layer an internal

longitudinal and an external transverse layer of muscular fibres.

Muscles.—In accordance with the presence or absence of muscles in the walls of the veins, these vessels are divided into the muscular and the non-muscular.

To the former belong the veins of the pia and dura mater, the veins of Breschet in the bones, the veins of the retina, the lower portions of the veins of the trunk opening into the vena cava superior, the external and internal jugular veins, the subclavian veins, and the veins of the maternal portion of the placenta.

In accordance with the arrangement of the muscular tissue, the veins may be divided into three groups; namely,—

Veins with longitudinal muscles, as those of the pregnant uterus.

Veins with an internal layer of circularly, and an external layer of longitudinally arranged muscular fibres of which examples are found in the vena cava inferior, both in and below the liver, the vena azygos, and the portal, hepatic, internal spermatic, renal, and axillary veins.

The third group includes veins possessing an internal and an external longitudinal and a middle transverse layer of muscular fibres. Amongst these are the iliac, crural, and popliteal veins, the branches of the mesenteric veins, and the umbilical vein.

A fourth group includes the veins with circular muscular fibres, to which the veins of the upper and partly of the lower extremities, the smaller veins of the neck, the internal mammary vein, and the veins in the substance of the lungs belong.

The arrangement of the muscles is thus seen to vary even in the same vascular region. The middle-sized branches of the mesenteric veins contain, for instance, two longitudinal muscular layers with an intermediate circular layer, whilst, on the other hand, the vena porta possesses a feebly developed internal layer of circular fibres, and an external longitudinal layer of considerable thickness.

As regards the proportionate strength of the muscular coat, the veins of the lower extremity and vena umbilicalis occupy the first rank; and then follow in succession those of the abdo-

minal viscera, and of the upper extremity, which are about upon an equality; and finally those of the thorax and neck.

The longitudinal muscular coat is most developed in the inferior vena cava below the liver, in the iliac, portal, renal and mesenteric veins.

The thoracic portion of the inferior vena cava has no contractile fibres in man, the ox, sheep, pig, and rabbit, whilst the hepatic portion of the same vessel in these animals possesses a strong circular muscular layer.

In the superior vena cava of man, in opposition to that of the ox and sheep, there are no muscular fibres, and they first appear in the upper branches of the common jugular vein. Here, in consequence of the fixed position of the vessels, those obstacles are absent which render the passage of the current in the inferior cava difficult. On the other hand, according to Remak, in the superior cava of the ox and sheep there are internal transverse and external longitudinal muscles, an arrangement that may, perhaps, be rendered requisite by the different position in which the head is maintained.

The Tunica Adventitia of the veins, like that of the arteries, consists of bundles of decussating fibrils, the direction of which is for the most part longitudinal. As a general rule their diameter increases with that of the vessel, but there are many exceptions. The tunica adventitia of the veins is distinguished from that of the arteries by its greater thickness and the small amount of elastic fibres it contains, as well as by the presence of longitudinal muscles in certain vessels. The external layer of longitudinal muscles belongs exclusively to the tunica adventitia. To whatever extent the longitudinal fibres may be developed, they never form a distinct coat as in the tunica adventitia of arteries, but only a coarse network constructed of larger or smaller fibres, which are chiefly found in the middle and internal layers of the tunica adventitia, and diminish towards the outer. The limits between the layers of muscular and elastic fibres are never very well defined.

The Valves of the Veins cannot be regarded as true duplications of the internal tunics. The elastic finely fibrillated

internal membrane covers only the convex surface of the valves. The proper substance of the valve is composed of finely fibrillated connective tissue with stellate and fusiform cells.

The muscular fibres which have been described by Wahlgren in the larger valves, I have not been able to discover with certainty.

The sacciform transparent appendages of the veins on the cardiac side of the valves of the veins (to be found in the axillary external and internal jugular and crural veins, as well as in the other branches), which, according to Remak,* consist exclusively of bundles of smooth muscular fibres, I find are not contractile.

Capillaries.

Capillary vessels removed from living adult animals, and examined with due precaution, as, for example, those of the hyaloid membrane of Frogs, treated with the fluid of the aqueous, appear to be composed of a delicate, double-contoured, dull membrane, in which oval nuclei are imbedded at tolerably regular intervals. The parietes of these tubes are therefore not structureless. The capillaries of the hyaloid of the Frog appear to consist of a soft cloudy substance which in no respect differs from the substance of the delicate threads of protoplasm given off by the cells of the tunica adventitia. In young living animals, as in tadpoles, we may still more easily convince ourselves that the capillary wall is not completely structureless, but that granules are distributed through it in a stellate manner, and that in its general appearance it closely resembles protoplasm. The wall here frequently appears uneven and provided with small teeth, or prolonged into fine partly solid and partly hollow funnel-like and, for the most part, non-nucleated pointed processes. The substance of these is always more granular than that of the rest of the membrane.

Such lateral processes are found also in adult animals, Stricker† having seen them in the nictitating membrane of the

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* *Uber contractile Klappensäcke an den Venen des Menschen, Deutsche Klinik*, iii., p. 32, 1856.

† *Sitzungsberichte der Wiener Akademie,* Band xii.

Frog, whilst I have also observed them in the hyaloid. Threads of a similar nature occasionally form connecting bridges between neighbouring vessels. The diameter of these processes is often far less than that of the capillary from which they spring, and is insufficient for the passage even of a single blood corpuscle. These outgrowths, which act as vasa serosa, and as the youngest sprouts of growing capillaries, render it highly probable that even in adult animals a new formation of vessels occurs, though, perhaps, only to a limited extent.

In many and especially in large recently formed capillaries, whether produced under normal or under pathological conditions, as, for example, in the membrane capsulo-pupillaris, the wall may be almost immediately broken up into finely granular fusiform protoplasmic masses.

A similar cellular structure may be rendered apparent in the

Fig. 49.

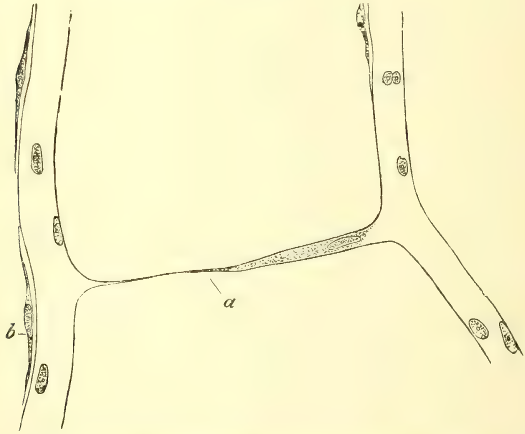

Fig. 49. Capillaries from the membrana hyaloidea of the adult Frog, showing a thread-like solid anastomosis between them. *a b*, cells belonging to the tunica adventitia.

capillaries of adult animals by various modes of preparation. Thus Klebs* observed that in the urinary bladder of the Frog, after treatment with phosphate of soda, the nuclei of the capil-

* Virchow's *Archiv*, Band xxxii., p. 172, 1865.

laries were invested by a cloudy layer of protoplasm, which formed elongated fusiform bodies partly lying on the surface an d partly imbedded in the substance of the membrane Nearly coincidently in point of time, and apparently independently of each other, Hoyer,* Auerbach,† myself,‡ and Aeby,§ and more recently Chrzonszczewsky,|| have by means of nitrate of silver shown that the wall of the capillaries is divisible into nucleated areas. The action of the nitrate of silver is to colour the substance intervening between the cells of a brown or black tint, by which means the individual cells are brought into strong relief, and may be then isolated by treatment with a solution of potash containing 35 per cent. of the alkali (Aeby, Eberth).

A cellular structure was subsequently shown to exist in the wall of the capillaries in almost all the organs of vertebrate as well as of many invertebrate animals, both by myself ¶ and by Legros.**

The plexus demonstrated by Federn†† in and upon the capillary walls, after treatment with nitrate of silver, is entirely different from the foregoing, from which it is distinguished by the irregularity of its meshes. Its nature has not been satisfactorily ascertained. The form of the cells lining the capillaries varies to a considerable extent. As a general rule, it is different in vessels of different calibre. Small capillaries present cells that are more fusiform in shape; large capillaries,

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* *Archiv für Anatomie*, dated Jan. 18, 1865.

† Breslauer, *Zeitung*, Feb. 17, 1865.

‡ *Sitzungsberichte der Physikal. Medicin. Gesellschaft zu Würzburg*, Feb. 18, 1865; *Medicinisches Centralblatt*, No. 13, 1865; *Uber den Bau und die Entwickelung der Blutcapillaren, Erste Abhandlung*, "On the Structure and Development of the Blood Capillaries, First treatise;" *Würzburger Naturwissenschaftliche Zeitschrift*, Band vi., 1866.

§ *Medicinisches Centralblatt*, No. 14, 1865.

|| Virchow's *Archiv*, Band xxxv., 1866.

¶ *Loc. cit.*, *Ueber die Capillaren der Wirbellosen*, "On the Capillaries of Invertebrate Animals."

** Legros, *Note sur l'Epithelium des Vaisseaux Sanguins*, "Note on the Epithelium of the Bloodvessels," *Journal de l'Anatomie et de la Physiologie, Cinquième Année*, 1868, p. 275.

†† *Sitzungsberichte der Wiener Akademie*, Band liii., 1866.

cells that are more polygonal. After treatment with nitrate of silver, the cells appear bounded by sinuous outlines that are often crenulated and lobed; as, for example, in the pulmonary

Fig. 50.

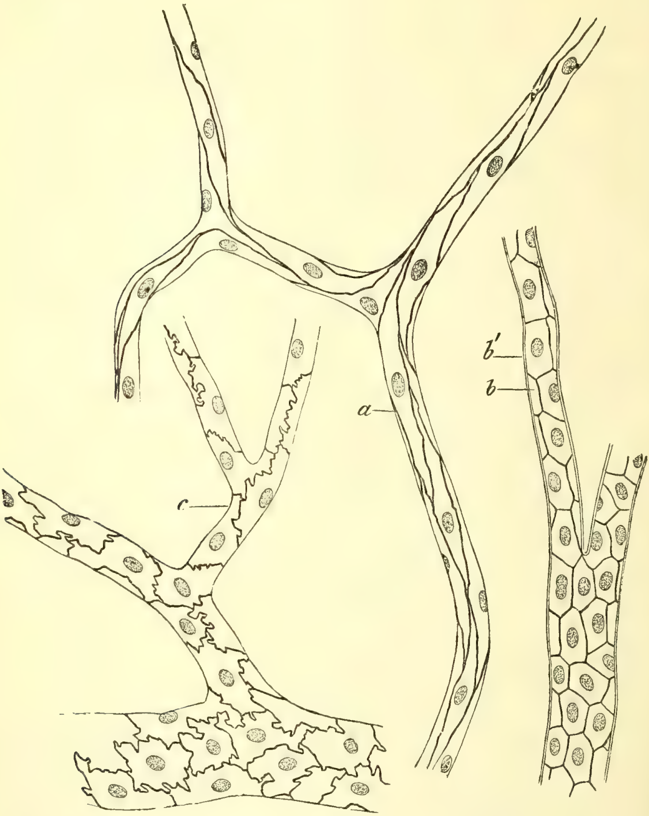

Fig. 50. *a*, Small capillaries with fusiform cells, taken from the mesentery of Leuciscus; *b*, capillaries of the pecten of the eye of the Bird, exhibiting polygonal cells; *b′*, hyaloid membrane investing the capillaries; *c*, capillaries from the intestine of the Snail, showing irregularly lobed cells.

capillaries of the frog and of mammals, in the capillary veins of the choroid of the rabbit, and in the capillaries of cepha-

lopods. The dark contour lines often exhibit larger or smaller knot-like swellings. Many of these are composed of less deeply tinted substance, surrounded by the intensely brown cementing material, and perhaps consist of some modification of the latter, which is feebly acted on by nitrate of silver.

The slighter staining may, however, also depend on diminished thickness of the cement, whilst the deeper tints of other parts may proceed from the presence of particles of albumen, belonging to the original contents of the vessel, being retained in small indentations of the cell membrane, and becoming of a deep brown colour by the action of the silver.

That the dark lines winding round the nuclei in the silvered

Fig. 51.

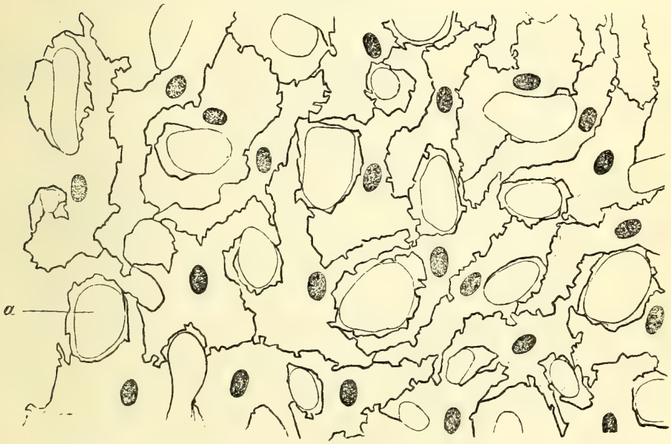

Fig. 51. Capillaries of the lungs of the Frog, with irregularly dentated cells. *a*, vascular meshes.

wall of the vessel are not due merely to albuminous precipitates occurring in the small furrows surrounding the several cells, as Auerbach* appears willing to admit, seems to be sufficiently refuted by the reactions of the cement in other membranes composed of cells, to which no application of nitrate of silver has been made. Besides the above-described dark inter-

* Virchow's *Archiv*, Band xxxiii., 1865, p. 380.

vening portions, clear areas of various size are also observable, interposed between the plexuses of lines. The margins of these are, for the most part, similarly dentated to those of the adjoining cells, but they are always of smaller size, and destitute of nuclei.

These appearances are not so frequently met with in the capillaries of mammals, but are common in the large arteries and veins, and also in the vessels of lower animals; as, for example, in the Cephalopods. Many of these non-nucleated areas (intercalated areas, as Auerbach calls them), may fairly be regarded as portions of the vascular cells which have been pinched off.

Small, irregularly shaped, dark, sharply defined spaces may, after treatment with nitrate of silver, be met with within as well as between the cells.

The number of the dark and clear intermediate areas varies much in different individuals, and more in the arteries and veins than in the capillaries. It has not been clearly proved that they are actually spaces in the wall (Stomata of Cohnheim). To enable us to understand the passage of blood corpuscles through the vascular walls, it is not requisite that coarse spaces or openings should exist, provided we may regard the vessel as composed, not of a stiff, but of a soft material, forming an elastic and permeable membrane. If the openings were really coarse, colouring particles of large size would pass through the vascular wall in various regions. But this never occurs. We do indeed see that fine colouring particles* escape through the vascular wall, but this does not occur easily with those possessing the diameter of the colourless blood corpuscles. These, on the other hand, by reason of their softness and elasticity, accommodate themselves to the fine invisible pores of the vascular membrane, and having traversed these, regain their original form.

Their escape must not, however, be regarded as a simply passive process, like the filtration of a colloid substance, to which it was likened in the first instance by Hering;† for it

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* W. Reitz, *Sitzungsberichte der Wiener Akademie*, Band lvii., 1868.

† *Wiener Sitzungsberichte*, Band lvii., 1868.

can be influenced in the most various modes by the contractility of the cells. Everything, in fact, which favours or checks their active motility influences their extravasation (Hering).

The finer capillaries consist only of a tube composed of cells or of a cylindrical layer of protoplasm. As the capillaries

Fig. 52.

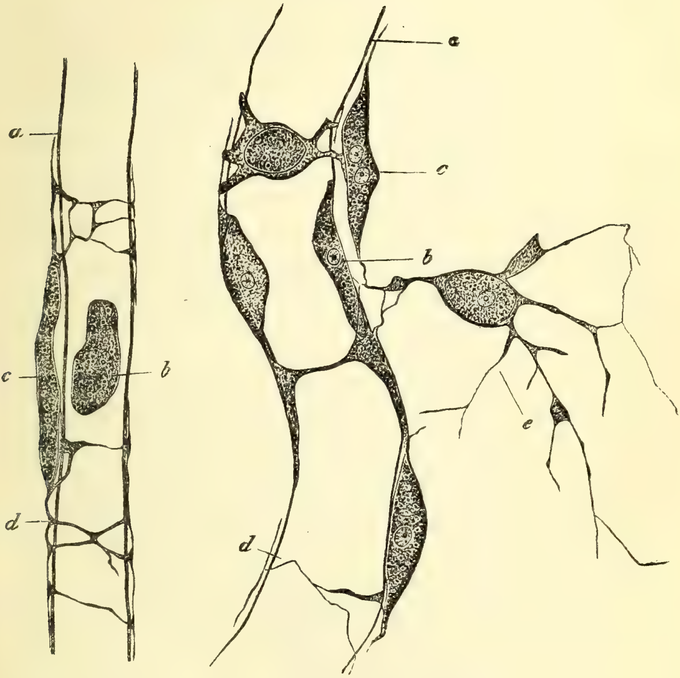

Fig. 52. Capillaries from the hyaloid membrane of the Frog. *a*, capillary wall; *b*, nucleus of the same; *c*, cells of the tunica adventitia; *d*, processes of these cells clasping the capillary wall; *e*, stellate cells anastomosing with the cells of the tunica adventitia.

become larger, a delicate tunica adventitia is superadded, which, in the hyaloid membrane of the frog (a membrane well adapted for this investigation), is formed, according to the

researches of Iwanoff* and myself, of a delicate network of fine fibrils, composed of the processes of stellate cells lying directly upon the vascular wall. Each of these cells consists of a large elongated nucleus, invested by an extremely delicate layer of protoplasm.

Chronsczczewsky† observed, in capillaries which had been treated with nitrate of silver, the cells detached from their connections, and at the same time the external wall of the capillary prolonged over the hiatus. However little evidence there may be against the presence of a tunica adventitia in the capillaries of other organs, I must still remark that such observations as the above, for reasons that I cannot here discuss, are not always conclusive.

Between the capillaries of the hyaloid of the Frog isolated stellate cells occur, with round nuclei and delicate protoplasm, branching off into many processes which often anastomose with the processes of the cells of the tunica adventitia. Towards the small arteries and veins the pericapillary plexus becomes constantly closer, and soon in its stead there appears a delicate transversely folded and nucleated membrane, which is sometimes elevated in the form of small vesicles.

The general structure of these parts renders it scarcely probable that, as Iwanoff admits, the capillary sheath constitutes a lymph space.‡ Numerous examinations of the tunica adventitia of the larger hyaloid vessels, treated with nitrate of silver, and undertaken with the view of detecting the indications of cells in it, have led, in all instances, only to negative results.

A similar nucleated membrane forms the outermost covering of the larger-sized capillaries, and of the arteries and veins of

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* *Medizinisches Centralblatt*, No. 9, 1868.

† Virchow's *Archiv*, Band xv., p. 172, 1866.

‡ In my first treatise I described the capillaries of the pecten in the eye of the bird as possessing a delicate double-contoured tunica adventitia resembling the structureless membrane of certain gland tubes. More recently I have satisfied myself, from transverse sections of the pecten, that the apparent tunica adventitia is only the hyaloid membrane which invests the whole of the pecten, and from its exactly following the course of the vessels, gives, when seen on the flat, the illusory appearance of a complete tunica adventitia.

the brain, spinal cord, and retina of man. The action of nitrate of silver frequently brings into view irregular flat cells in their substance, which are often fused into one another. By careful treatment they may be obtained in the isolated condition.

Fig. 53.

Fig. 53. A rather large capillary from the hyaloid of the Frog, presenting a membranous and nucleated tunica adventitia.

This layer may be distinguished as the *external vascular epithelium*, or still better as the *vascular perithelium.*

The number of cells seen on a transverse section of a capillary tube is, with few exceptions, dependent less on their size than on their form, because the size of the cells *in the capillaries* corresponds with the calibre of the vessels. In the

simplest examples, a fusiform spiral cell presents itself, the lateral surfaces of which are in contact, whilst the extremities occupy the spaces between the ends of adjoining cells. The capillaries in the pecten of the bird, even when extremely delicate, possess small polygonal cells, the breadth and length of which are nearly equal. It is only occasionally, and in the larger vessels especially, that the cells are distinctly fusiform.

As concerns the substance of which the cells are composed, it is always more abundantly and distinctly granular towards the centre and around the nucleus, whilst near the margin it is quite clear, and thins off to a delicate border. The capillary cells of the pecten of the bird, on the other hand, are, even in profile, only indistinctly fusiform, are of nearly equal thickness at the centre and at the margins, and consist of finely granular protoplasm, with a simple or divided nucleus, the contents of which frequently separate from the investing membrane of the nucleus, in the form of a roundish spherule, resembling a large nucleolus.

Only a few vascular regions form an exception to these statements; namely, the capillaries of the liver of Mammals and Amphibia, the chorio-capillaries of the former class, the hyaloid of frogs, and the young capillaries of the tadpole, and of pathological products of recent formation.

After repeated observations, I have only been able to discover the presence of cells in the capillaries in these instances, in a few isolated points; but in their stead I found fusiform or branched nucleated areas on the walls, bounded by finely punctated or interrupted lines. In the chorio-capillaris and the hyaloid membrane of the frog I found fusiform or polygonal cells in some only of the coarser capillaries, whilst in others no trace of them was discernible.

As regards the significance of these facts, three possibilities exist, either the capillary wall does not consist of cells at all, or, if this be the case, they have disappeared in consequence of fusion with one another, or the capillary wall has become only imperfectly differentiated into cells.

Now if, after repeated examination, a cellular structure is only demonstrable in the stronger and older capillaries, and but rarely in the younger, the conclusion is admissible, that

all capillaries are not constructed alike, and that they are not altogether intercellular tubes. Supposing that a nucleated or a non-nucleated, and in the first instance solid, process elevates itself from a capillary wall, gradually becomes elongated and hollow, its cavity communicating with the lumen of the capillary,—this may, in favourable cases, be regarded as a funnel-shaped outgrowth from a cell, but it is not an intercellular passage. In many instances, as in tadpoles, such outgrowths from capillaries are discoverable, which present no trace of cellular structure when treated with nitrate of silver, although in older vessels they can be readily brought into view. Must we not consequently conclude that the capillary wall thus beset with processes, is similarly composed to the funnel-like projections, and that, as Stricker says, they are composed of protoplasm, which has assumed a tubular form?

The capillary wall is contractile both in young and in adult animals. Stricker* saw the capillaries, not only of tadpoles, but of the nictitating membrane of frogs, contract to such an extent, that not even a single file of blood corpuscles could traverse them. Lastly, he observed small loop-like projections raise themselves from the wall of the capillaries of the nictitating membrane, and again become retracted. It is not improbable that it is by means of such contractions the corpuscles are pressed into the capillary wall, and ultimately made to traverse them.

Cavernous Vessels, Lacunar Blood Paths, Vascular Plexuses.

Cavernous vessels result from the unravelling of the vascular wall, which becomes converted into a spongy tissue; or from its becoming fibrous and membranous towards the lumen of the vessel, giving off processes that intercommunicate with each other, and which either form a spongy layer on the inner surface of the vascular wall, or a plexus traversing its entire calibre. A similar result is obtained from the occurrence of quickly consecutive anastomoses of vessels of various size. The

* *Wiener Sitzungsberichte*, Bände li. and lii.

primary vascular wall becomes teased out into thin trabeculæ and plates, varying in thickness, which are sometimes formed of simple cellular threads, and sometimes of all the tissues entering into its composition.

Structures of this kind are rarely met with in the arteries. The so-called carotid gland of the frog is, however, an example of it. In this instance, the strong muscular wall of the carotid artery forms internally a network of trabeculæ, enclosing spaces of variable size, which communicate freely with one another and with the lumen of the vessel. These trabeculæ are simple outgrowths of the vascular wall, containing muscle cells, which chiefly run in the oblique and longitudinal direction. I cannot corroborate the statement of Leydig, that these are transversely striated, but they are certainly much stronger than other muscles entering into the formation of vessels.

A similar structure has been found by Retzius to occur in the pulmonary arteries and aorta of the turtle.

The structure of cavernous veins consists, in some instances, of simple trabeculæ of connective tissue, as in the cavernous sinus, whilst in others it contains, in addition to the connective tissue, bloodvessels and muscular bundles running longitudinally, and anastomosing with one another, as in the corpora cavernosa of the generative organs. The endothelium of the vessels forms the innermost layer of these blood cavities.

The cavernous capillaries repeat, on a small scale, the relations of the cavernous veins. In the pulmonary organs of the snail the blood cavities are traversed by delicate nucleated trabeculæ, composed of fine homogeneous connective tissue. There is here as complete an absence of a cellular investment as in the great vessels of the lungs and heart.*

In the branchiæ of Crustacea the framework of the blood spaces is, on the contrary, composed of cells, the external expanded extremities of which rest immediately against the cuticle forming the so-called chitinogen layer, whilst the pyriform or clavate bodies of the cells which conceal the nucleus are applied

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* Semper, *Zeitschrift für wissenschaftliche Zoologie*, 1856. Eberth, *Blutgefässe der Wirbellosen*, "Bloodvessels of Invertebrates."

to the axes of the gill laminæ, and adhere to the wall of the larger branchial vessels. Between the cells are roundish spaces intercommunicating with one another, through which the blood courses. There is no special membrane lining or limiting these blood passages.*

Fig. 54.

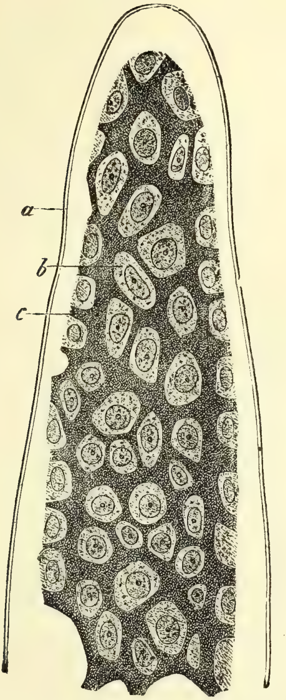

Fig. 54. Gill lamina of the River Crab. *a*, cuticula; *b*, clavate cells; *c*, lacunar passages for the blood in the interspaces of the cells. Surface view.

Cavities similar to these, through which the blood courses, are also found, according to Wilhelm Müller, in the spleen of mammals.

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* Häckel, Müller's *Archiv*, 1857. Leydig, *Lehrbuch*, 1857, p. 385. Eberth, *loc. cit.*

In the process of reparation of a wound there also originate finer or coarser intercellular blood paths, destitute of definite walls, which occupy the interspaces of the granulation cells. Originally they form an intermediary plexus of plasmatic canals which are supplied by the arteries,—the blood issuing through spaces in the unravelled vascular wall, and being similarly discharged into the veins. A portion of these plasmatic canals subsequently expand into true bloodvessels, the walls of which are formed by the fusion of the cells lining the blood canals; the greater number, however, disappear altogether.*

Certain vascular plexuses are closely allied to the cavernous tissues, and, indeed, not unfrequently, as in the case of the papillæ of the comb of the cock, develop into actual cavernous spaces. Amongst these vascular plexuses there is one which lies in front of the coccyx in man, and deserves special notice, from the peculiarities of structure it presents, and to which it owes the names it has received from its discoverer, Luschka,† of coccygeal gland, and nervous gland.

This plexus forms a round or slightly oval, pale red, compact body, of at most 2·5 millimeters in diameter, the surface of which is either smooth or slightly tuberculated. Sometimes, instead of this single body, there may be found from three to six poppy or millet-seed sized masses, connected together by loose connective tissue, and seated on fine branches of the middle sacral artery. According to their discoverer, these bodies consist of fibrillar connective tissue, with numerous oblong nuclei, containing closed roundish vesicles, and simple or branched slightly varicose tubes, which are composed of a delicate structureless basement membrane, lined by an epithelium-like layer of

* Thiersch, *Artikel Wundheilung*, "Reparation of Wounds," in Pitha's and Billroth's *Handbuch der Chirurgie*, pp. 553 and 555.

† *Steissbeindrüse oder Nervendrüse des Beckens*, "Coccygeal Gland or Nervous Gland of the Pelvis," *Archiv für Pathologische Anatomie und Physiologie*, Band xviii., p. 106, 1860. *Der Hirnanhang und die Steissdrüse des Menschen*, "The Pituitary Body and Coccygeal Gland of Man." Berlin, 1860. *Anatomie des Menschlichens Beckens*, "Anatomy of the Human Pelvis." Tübingen, 1864, p. 187.

round or slightly polygonal cells, replaced in recently born animals by true ciliated epithelium. The rich supply of nerves to these supposed glands, and especially of sympathetic fibres, and their position near the lower extremity of the great sympathetic, appears to justify the view that whilst the hypophysis is the cerebral pole of the sympathetic, this gland constitutes the anal pole, and is to be regarded as a nervous gland.

Luschka's statements, so far as regards the presence of gland vesicles and tubes, have recently been corroborated by Krause.* Arnold,† however, calls the glandular structure of this organ in question, pointing out that the glandular bodies of the middle sacral arteries are capable of being injected, and that they only represent ampullar and fusiform dilatations of the lateral and terminal branches of that artery; in other words, a true plexus arteriosi coccygei.

These vascular sacculi, which may already be found as small, partial, but true aneurisms in the course of the middle sacral artery, and in larger number enter into the composition of the coccygeal gland, consist, according to Arnold, of an investment of connective tissue, which covers a layer of concentrically arranged and obliquely coursing muscular fibres, within which again is a delicate structureless coat, resembling the elastic fenestrated membrane. The innermost layer, the epithelial-like coat of the gland vesicles and tubes of Luschka, is composed of fusiform and polygonal cells, which frequently overlap each other at their edges. The connective intervening substance of this is rich in muscles, which run in the most diverse directions, and form a continuous layer on the surface.

At a later period Arnold discovered the existence of similar structures, consisting partly of vascular sacs, and partly of retia mirabilia, in the course of the middle sacral artery in the dog, cat, otter, squirrel, rabbit, rat, horse, ox, and pig.

Krause and Meyer‡ have therefore corroborated the princi-

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* *Zeitschrift für rationelle Medicin*, Band x., 3 R., p. 293. *Anatomische Untersuchungen.* Hannover, 1860, p. 98.

† *Archiv für Pathologische Anatomie*, xxxii., p. 293, 1865; xxxv., p. 454, 1866; xxxix., p. 220, 1867.

‡ *Zeitschrift für rationelle Medicin*, xxviii.

pal statements of Arnold, but, at the same time, have established the occurrence of a laminated epithelium lining the interior of the vascular sacs, and have pointed out the analogy of these with the carotid glands of the frog, and termed them caudal hearts.

The subject has again been taken up very recently by Sertoli,* and the results of his inquiries are not in accordance

Fig. 55.

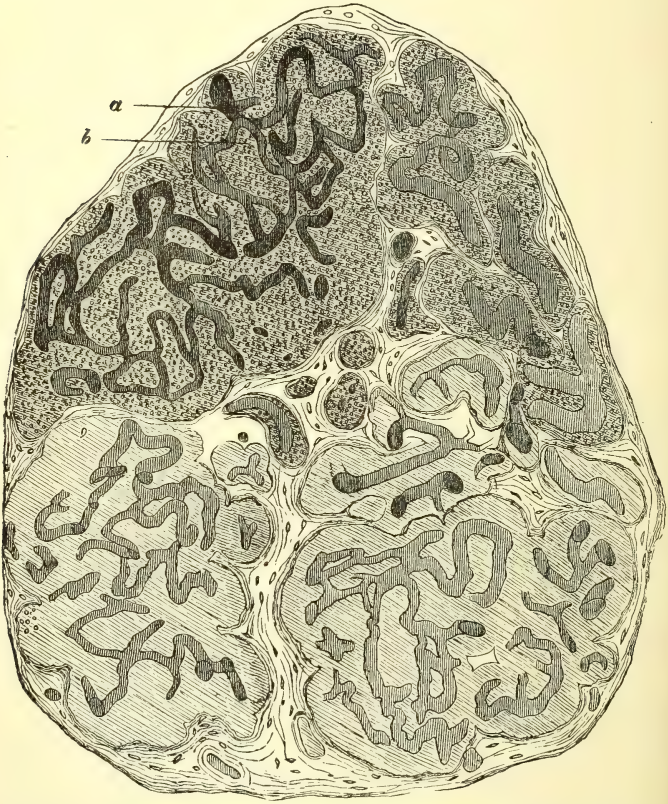

Fig. 55. Section of a naturally injected coccygeal gland. *a*, vessels; *b*, collection of cells.

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* *Archiv für Pathologische Anatomie*, Band xliii., p. 380.

with those of the previous observers. He finds that the stroma of the so-called coccygeal glands is formed of a tough, fibrous, richly nucleated connective tissue, traversed by bundles of smooth muscles, and containing rounded and elongated tubes, the walls of which are principally composed of fibres of connective tissue, running in a longitudinal direction, with, at most, a few isolated muscle cells distributed amongst them. These tubes become filled with polygonal cells, which, in concentric series of several layers, surround one or more centrally situated capillaries, or, less frequently, fine arteries or veins. These vessels are for the most part of normal calibre, and are rarely dilated; but when they are so, it is probably the result of manipulation.

My own view is that the coccygeal gland is a plexus of

Fig. 56.

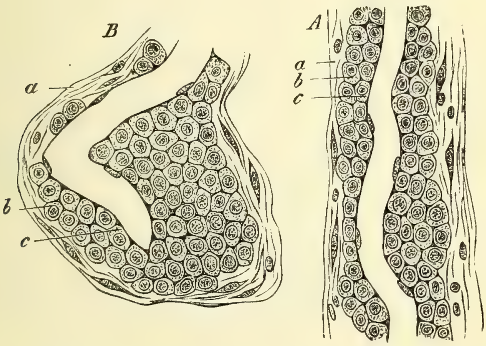

Fig. 56, A. Cellular vascular sheath, from the coccygeal plexus. *a*, connective tissue with scattered cells and nuclei; *b*, round and polygonal cells lying immediately upon the capillary wall *c*.

B. A capillary from the coccygeal plexus, with a vascular sheath very rich in cells. References as in A.

vessels which are sometimes of equal width, and sometimes slightly dilated, or varicose, with lateral dilatations, which lie in a stroma of connective tissue, the numerous round, oval, and fusiform cells of which are certainly only in very small proportion muscular. The greater number of these vascular sacs are found in the capillaries and veins, and seldom in the

arteries. Their number and size is often so considerable that true cavernous spaces are formed, and the intervening substance is reduced to a thin framework.

Around these vessels, and immediately external to their delicate cellular internal membrane, which is identical with that of the ordinary capillaries, lie rounded and elongated heaps of slightly polygonal cells, which are never invested by a definite structureless membrane, but have only a layer of connective tissue with longitudinal fibres on their outer surface. Many capillaries are invested, and frequently for considerable tracts, with a single layer of these cells, which are covered by a fibrous tunica adventitia containing numerous nuclei.

Small groups of similar cells lie also more remote from the vessels in the matrix or intervening substance. The larger cell masses must therefore be regarded as richer collections of these scattered through cellular vascular sheaths.

The size of these cell masses diminishes in proportion to the development of the vascular sacculi.

On one occasion I found in the cell masses laminated structures similar to those found in the granules of the thymus.

The intervascular tissue of the coccygeal gland is very rich in nerves. As regards the ganglion cells, which Luschka stated he had observed, neither Arnold, Krause, nor myself have been able to satisfy ourselves of their presence. Nor have I been more fortunate in obtaining a view of the club-shaped terminations of the nerves resembling Pacini's corpuscles, or terminal bulbs, described by Luschka. They are said to be 0·8 millimeters broad, and to possess a thick membranous and fibrous investing sheath containing numerous longitudinal nuclei.

Inasmuch as a glandular structure is not demonstrable in the so-called coccygeal gland, which rather appears to consist of a rich plexus of for the most part capillary vessels, invested by a cellular sheath, some of which are normal, whilst others are dilated in a fusiform or sacciform manner, it is clear that for the future it should be named the plexus vasculosus coccygeus, and that it should be classed with the carotidean vascular plexus of the so-called carotid gland, at the upper extremity of the common carotid of man and mammals.

CHAPTER IX.

THE LYMPHATIC SYSTEM.

BY PROFESSOR F. v. RECKLINGHAUSEN.

IN consequence of the pressure under which the blood courses through the vessels of the several organs of the body, the tissues are constantly permeated with serous fluid, which partly furnishes the materials requisite for their nutrition, and is in part also subservient to the preparation of the secretions. This serous or tissue fluid requires constant renewal, a rapid exchange of material, without which it quickly alters the composition of the various tissue elements around which it plays. The passage of fresh fluid from the blood into the tissues would, however, cease as soon as the pressure of the latter approximated that under which the blood moves in the vessels, were not a constant escape of the fluid provided for by means of a canal system, which is so far separate from the bloodvessels supplying the tissues, that the pressure of the blood is not transmitted directly into the canal system—that is to say, not with its full force. These canals, the lymph vessels, form therefore a peculiar system, the rootlets of which are distributed through the tissues, and which only so far stands in connection with the bloodvessels, that it, 1st, indirectly withdraws from them the fluid they contain, and, 2nd, that it ultimately returns that fluid to the bloodvessels by its terminal trunks. The origin of the lymphatic system is in relation with the capillary vessels in which the blood moves under a considerable pressure; its termination, on the other hand, communicates with the chief venous trunks, and consequently with those parts of the vascular system in which the blood pressure descends to its minimum amount, and is in fact almost reduced to zero.

The difference in the amount of these two pressures constitutes an essential factor in the production of the movement of the lymph; so that the greater the difference, the more rapid is the movement. The lymphatic vascular system borrows its contents, as well as the impulsive force under which they move, from the blood vascular system; and in so far it may be regarded as an appendage of, or as an accessory closed system to, the blood vascular apparatus.

The dependency of the lymphatic system on the bloodvessels is indicated by the circumstance that, as a general rule, the lymphatic system in any organ is so much the more strongly developed in proportion as its supply of bloodvessels (mucous and serous membranes, skin, glands) is more abundant; but there are also organs characterised by a peculiar richness in lymphatic vessels, which are at the same time especially adapted for absorption (gastric and intestinal mucous membrane, central tendon of the diaphragm).

The entire lymphatic system may be divided into two sections; the first containing the fluid which, immediately after its escape from the bloodvessels, circulates around the several elements of the organs, the interstitial serous spaces; and, secondly, the system of the efferent canals, the proper lymphatic vessels. This second section will be here first described, because its structure is much more accurately known.

The efferent canals, or *lymphatic vessels,* ordinarily agree in their form, arrangement, and in the structure of their walls with the bloodvessels. In the greater number of organs they form plexuses, which are so much the more close, the more abundantly the tissues are supplied with bloodvessels: moreover they only occur in association with bloodvessels; and those tissues which are destitute of bloodvessels, like the cornea, vitreous humour, and epithelial tissues, possess also no proper lymphatics. Like the bloodvessels, they generally form cylindrical tubes, and only in certain regions, hereafter to be described, present the characters of fissures or lacunæ, under which condition, however, they not unfrequently form investing sheaths for different organs. The lymph vessels may be distinguished for the purposes of description into the smallest branches, the capillaries which are intercalated between the

system of the blood capillaries, and the larger lymph vessels which issue from the several organs, and ultimately unite to form the main trunks.

The *larger lymphatics* of Mammals and Birds are always tubes, the walls of which agree with those of the bloodvessels in their structure, and hence present a tunica intima very rich in elastic fibres, and lined by a single layer of tesselated epithelium; a tunica media, consisting exclusively of muscular elements; and a tunica adventitia, composed as usual of loose connective tissue. The tunica media does not attain the thickness of that in the arteries, but its fibres pursue a similar transverse direction. Upon the whole, the lymphatics are not so thick-walled as the arteries, but, in the relation between the thickness of the wall and the calibre of the vessel, assimilate much more closely to the veins. The form of the lymphatics of Birds and Mammals is peculiar, and so far differs from that of the bloodvessels, that they are provided with very numerous valves, resembling generally the valves of the veins. Immediately above each valve the vessel is somewhat wider than just below, and not unfrequently there is a distinct saccular dilatation at this point. As a consequence of this arrangement, the lymphatics only preserve their cylindrical form for short distances in those parts which are destitute of valves, whilst in those parts where the valves are numerous they assume a varicose or moniliform appearance. The valves, like those of the veins, are simply duplicatures of the tunica intima.

The structure and arrangement of the larger lymphatics present essentially different features in the Amphibia. They do not here form even approximatively cylindrical tubes, but *lacunæ*, which occupy the interspaces between the several organs. If, in consequence of an arrest of the flow of the lymph, or by artificial injection, they become more completely filled than is natural to them, they swell out in the form of large sacs, which, however, possess no constant or definite form, since they only represent interstitial spaces. As a general rule they do not possess an independent thick wall, capable of being detached from the surrounding parts, but their limits or boundaries are formed by the fasciæ and such condensed layers of connective tissue as are found on the surface of the different

organs, the surface which is turned towards the interior of the cavity being covered with a single layer of tesselated epithelium. Only such septa as divide the several lymph spaces from each other, and are composed of pure connective tissue, can be regarded as properly belonging to them. The lymph sacs in these animals therefore resemble the peritoneal and pleural sacs, with this difference, that the lymph sacs communicate with one another by means of microscopic openings in their septa, and consequently form a continuous system of cavities. Inasmuch as the lymph sacs are almost entirely destitute of proper walls, the muscular elements, the function of which is to aid in the propulsion of the lymph, also fail; but in their stead special contractile organs, acting rhythmically, appear in certain parts of the lymphatic system of Amphibia. These constitute the lymph hearts discovered by J. Müller, and one of them lying posteriorly near the sacrum propels the lymph into the sciatic vein, whilst the anterior pumps it into a branch of the jugular. They are chiefly composed of transversely striated short muscular laminæ.

These peculiarities in the structure and arrangement of the large lymphatics of Amphibia in contrast with those of other Vertebrata, are of great interest. They prove clearly that great variability occurs in the lymphatic system, much greater even than in the blood vascular system; and, in truth, this variability occurs not only in different classes of animals, but in one and the same species, and not only in the larger trunks, but in the smaller vessels. The number and size of the principal trunks of any organ, as, for example, of one of the extremities of man, presents as little constancy as the mode of their division. Even in one and the same organ the results of injection are often quite different, and it frequently happens that injections of the same organs in nearly allied animals present such remarkable differences, that only the most general statements can be made in reference to the arrangement of the lymphatics of any particular locality.* It is obvious, therefore, that those typical modes of arrangement which occur in the arterial and capillary blood vascular systems of the different organs can only be im-

* See the illustrations in L. Teichmann's *Saugadersystem*. Leipzig, 1861.

perfectly demonstrated in the lymphatics, and that only the general relations existing between the structure of any organ and its lymphatics present characteristic features. The varieties that occur in the arrangement of the lymphatics exhibit many peculiarities in certain regions of the smaller lymph vessels. Thus we see, in parts where they are very numerous and closely arranged, there are not unfrequently lacunar spaces even in Mammals, as if they had coalesced to form a flat and wide vessel; we meet also with a pair of lymph tubes accompanying a bloodvessel, and not unfrequently with regular sheaths, which partially or entirely surround them, as, for example, in the case of the chyle vessels in the mesentery of the Mouse (Brücke). In such instances as these we recognise in Mammals arrangements essentially similar to the lymph sacs of Amphibia.

There is still another circumstance that becomes intelligible from this comparison if we remember that certain sections of the lymphatic system of the Amphibia do not possess a tubular form, but represent ensheathing or lacunar spaces. They are thus analogous, as we have already seen, to serous sacs, and it will be understood how the latter stand in immediate relation with the lymphatic system, are in direct communication with it, and possess similar contents (see *infra*).

This variability of form recurs in the narrowest section of the lymphatic system, that is to say, in the *lymphatic capillaries*. For even amongst Mammals we meet in certain organs with lacunæ, representing the roots of the lymphatics; whilst in Amphibia the great majority of the lymph capillaries are tubular. The lacunæ correspond in form with the spaces between the parts of the organs they invest, such as the ducts of glands, etc. The capillary tubes, even in their finest branches, are provided with varicose enlargements, and these are often situated at the points of junction of the vessels, and occur so suddenly that transverse processes project into the lumen of the vessel, which are again so placed that they form a kind of valve. Such dilatations often succeed one another at very short intervals, especially in those lymphatics which immediately follow the capillaries, giving the impression of tubes constructed of a series of Florence flasks, of which each is inserted by its neck into the base of the one preceding it (see fig. 57). It is easy to

recognise, from the position of these processes, what direction the lymph current pursues in any particular vessel, since they are so arranged that, like the valves of the larger lymph vessels, they prevent any regurgitation of the fluid.

The arrangement of the capillary lymphatics in reference to the bloodvessels is a subject of special interest. The larger lymphatics run sometimes in immediate proximity to the arteries and veins, and sometimes separately, or, at all events, present no constant relation to them. But for the smaller and capillary lymphatics, the general statement may be made that they hold their course at as great a distance as possible from the blood capillaries. This characteristic feature may be most easily recognised in membranous expansions, in which the blood and lymphatic capillaries are distributed upon one plane: in such cases the points of junction of the lymphatic plexus always occupy the middle points of the meshes of the blood capillaries, and the converse. It is evident that this arrangement is most advantageous for the purpose of drainage. All fluid escaping from the blood capillaries must traverse the tisssue to reach the capillaries; and so long as this transudation occurs, a continuous play of fluid around all the tissues must take place. If, on the other hand, the lymphatic efferent canals lay in immediate contiguity to the blood capillaries; if the whole were not, so to speak, intercalated between the tubes of the lymphatic system and of the bloodvessels, the fluids might easily stagnate in those parts which were more remote from both, and a constant interchange of material would cease to take place. There is yet another point that is deserving of notice. In those membranes which present a free surface covered with an epithelium, as in the mucous and serous membranes and the skin, the lymph capillaries are found constantly to occupy a deeper plane than the bloodvessels. Whilst the latter ascend till they lie just beneath the epithelium, the lymphatic capillaries do not reach the uppermost stratum of connective tissue. These relations are most easily recognised in the membrane forming the web of the foot in the Frog, which is a duplication of the external skin; the lymphatics here exclusively lie in the middle connective tissue layer, whilst the bloodvessels course in the thin cutaneous laminæ

on either side. A similar arrangement of the two sets of vessels is strikingly shown in the case of the villi of the small intestine, in which the proper tissue of the villi forms a peripheric layer traversed by a close network of capillary bloodvessels, whilst the chyle vessel lies quite in the interior, near the axis, and is generally single and unbranched, as in the rabbit, ox, sheep, and man, though occasionally it has been observed to form a set of anastomosing capillaries, as in the dog, sheep, and ox. Again, if the results obtained from the injection of the cutaneous lymphatics by Teichmann, in a case of elephantiasis,* be considered to represent the normal distribution of the lymphatics, the capillaries of this system lie exactly in the centre of the papillæ of the cutis, whilst the blood capillaries traverse their periphery.

At first sight it appears remarkable that the lymphatics should lie so deeply in organs destined for absorption, as, for example, in the villi; this relation, however, is in itself a sufficient indication that the connective and other tissues of the villi play a most important part in the act of intestinal absorption, and that here also the central chyle vessel only acts as an efferent or drainage pipe. The function performed by the roots of plants is probably similar to that of the epithelium and the parenchyma of the villi. The chyle vessels, on the other hand, appear to be analogous to the vessels and fibrovascular tissue of the plant; if these were able to absorb, a more superficial position would be more appropriate to the discharge of their function.

Having now learnt the form and arrangement of the capillary lymphatics, we turn to the consideration of their structure, a question which has recently received particular attention, and has met with various answers. Are they, like the bloodvessels, provided with a proper wall, or are they destitute of a limiting membrane, constituting only lacunæ, or spaces in the tissues amongst which they lie? The decision of this question is particularly interesting in the case of the chyle vessels of the villi. The chyle formed after the ingestion of food containing abundance of fat owes its white colour to the

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* *Untersuchungen über das Saugadersystem*, Taf. 6, fig. 4.

presence of numerous extremely fine molecules, which are probably oil globules. Particles of a similar nature are met with during the process of absorption, both in the parenchyma of the villi and in the epithelial cells. In all probability, therefore, they press through the epithelial layer as undissolved

Fig. 57.

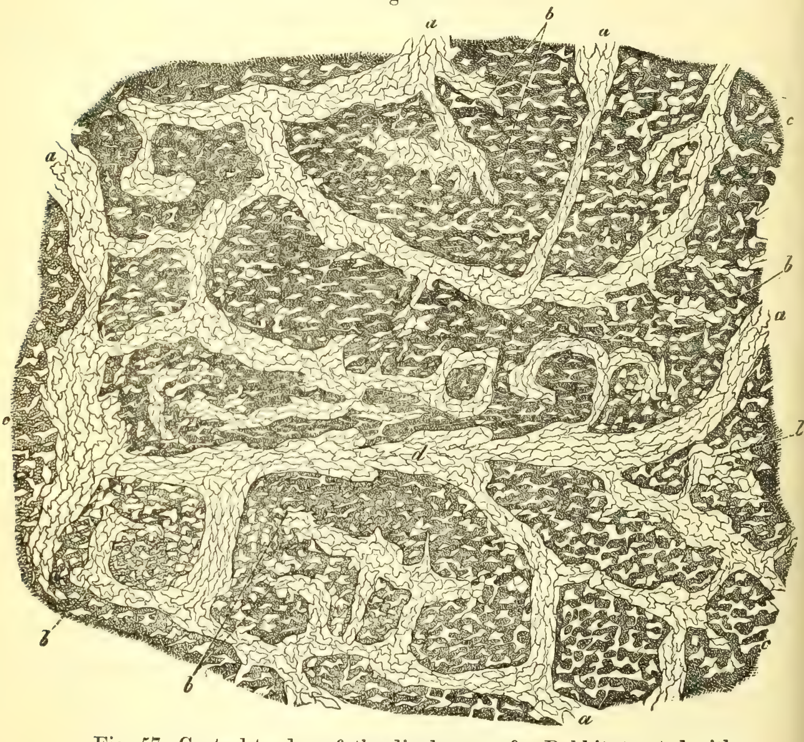

Fig. 57. Central tendon of the diaphragm of a Rabbit, treated with silver, and examined from the thoracic side. *a*, lymphatic capillaries with the contours of the epithelial cells; *b*, first appearance of the cells; *c*, connective tissue with serous canals; *d*, flask-shaped dilatations. Magnified 60 diameters.

molecules into the substance of the villi, and beyond this into the central lacteal. It would hence appear that the paths traversed by these minute oil drops in the periphery of the villi open directly into the central chyle vessel; and the sim-

plest view is, that no special limiting membrane exists (Brücke). On the other hand, microscopic examination shows that there is really a double, and not a mere single, outline to be seen in the central lacteal and in the finest capillaries in the tail of the Tadpole, from which the conclusion has been drawn that a homogeneous investing membrane is present (Kölliker). It was found also that in injected preparations the injection tightly filled the capillaries of the chyle and lymphatic vessels, without the escape of any of it into the surrounding tissues; and hence it was considered that the assumption was perfectly justified, that these vessels were as completely enclosed by an investing membrane as the bloodvessels themselves (Teichmann, Frey). In point of fact, the presence of a special membrane in the lacteals and lymphatics may be most easily proved by the application of the silver method of staining the tissues adopted by Recklinghausen. If a solution of silver be injected into the lymphatics as far as the capillaries, or if the tissues be generally impregnated with a solution of this salt, fine dark lines appear in the lymphatic capillaries (fig. 57), which are usually strongly looped or sinuous, including polygonal, or not unfrequently rhombic, areas, in all their peculiarities identical with the silvered lines of the most various epithelial tissues. The networks of silvered lines become visible as early as in the rather larger vessels succeeding the capillaries, where the enclosed areas are fusiform, and agree with those brought into view by the agency of silver on the inner surface of the large lymph and blood vessels. In the case of these last-named vessels, it may easily be proved that the lines in question depend on the presence of a single layer of flat epithelial cells lining the tunica intima; but, inasmuch as the same markings may be traced continuously into the lymphatic capillaries, it follows that these also possess a similar layer of tesselated epithelium.

In fact, even in the capillary lymphatics, subsequent treatment with carmine not unfrequently brings into view an oval nucleus in each area. Moreover, if the intestinal villi be torn off a few hours after death, we may sometimes meet with one from the centre of which a wide tube projects, consisting of flattened epithelial cells.

It is no longer, therefore, a matter of doubt that the *capil-*

lary lymphatics—at least, in those organs in which they have been investigated with special reference to this point, as the serous membranes, the walls of the intestine, the diaphragm, both in its muscular and tendinous portion, and the membrana nictitans of the Frog—*are lined by a single layer of flattened epithelium.* They also possess a special membrane, though not completely homogeneous and structureless, as was formerly maintained, nor entirely closed, as we shall hereafter have occasion to see.

I was formerly of opinion, after I had satisfied myself of the presence of an epithelium in the lymphatic capillaries, that I had by this means discovered an essential distinction between them and the blood capillaries ; but, as subsequently it has been shown by experiments with silver that the wall of the capillary bloodvessels, in some organs at least, consists of epithelial cells, the distinction fails.

The lymphatic capillaries are, in fact, constructed on the same type as the blood capillaries (see the section on the bloodvessels). The existence of such an analogy has been contested, because the blood capillaries can be easily isolated in portions of considerable length in some organs, as the brain, whilst it is very difficult to exhibit such detached portions of the capillary walls of the lymphatics. Very recently Frey has been led to the conclusion* that, "whilst in the blood capillaries the walls maintain a perfect independence in regard to surrounding tissues, in the lymphatics they fuse with them." I believe that we must beware of admitting that the blood capillaries are so completely isolable in all organs, or form such independent tubes, as in the brain. In many glands—as the liver, for example, not to mention the spleen—the wall of the capillary bloodvessels is not capable of being isolated.

And now arises the question, do the lymphatic capillaries possess a special wall or not ? Admitting an answer in the affirmative, are the above-mentioned phenomena taking place in the resorption of chyle consonant with it ? They would appear to demand that the lumen of the chyle capillaries should not be closed towards the free surface of the mucous membrane. But these appearances can be equally well explained, if we suppose that the wall is not everywhere formed of a continuous solid layer, or, in other words, that it possesses

* *Handbuch*, p. 427.

foramina. Up to a recent period it has been generally accepted that epithelial investments, except in the case of glandular epithelium, serve as a protection to the subjacent tissues, and therefore, by the intimate union of the cells with each other, form a firm, close tissue, permeable only for fluids. Since, however, the terminal apparatus of the sensory nerves has been discovered in the epithelial strata, and very recently also cup-shaped organs, both of which seem to be but ill adapted for protection, the epithelial tissues have gradually attracted more and more attention from histologists, and it is not surprising that further inquiries should be undertaken with the view of discovering other and peculiar arrangements. It is reasonable, therefore, on *à priori* grounds, to concede that the epithelial coating of chyle and lymphatic capillaries may present special peculiarities which stand in relation to the absorption of material from the surrounding tissues, and may, at any rate, at certain times, facilitate their passage. In some lymphatics, openings of appreciable size are already known to occur, through which, even during life, small bodies may be absorbed into the interior of the tube. They were first demonstrated by Recklinghausen, in the central tendon of the diaphragm. If we inject into the peritoneal cavity of mammals milk, blood, or fluids which have insoluble substances (consequently not carmine) in suspension, a beautiful injection of the network of lymphatics of the central tendon of the diaphragm may be obtained. If we press a cork ring against the central tendon from the thoracic side, attach a portion to it with needles, and then excise it, we are enabled to procure the surface of the tendon in an absolutely uninjured state. If now we place a drop of milk upon this, the absorption of milk globules into the lymphatic vessels may be directly observed under the microscope. The milk globules run towards certain points at which small vortices occur whilst they are penetrating into the subjacent lymphatics. The openings through which they gain entrance are only wide enough to admit two or three milk globules abreast, are roundish, sometimes even quite round, and represent, as is clearly shown by subsequent staining with nitrate of silver, spaces between the epithelial cells. They usually lead perpendicularly into the lymphatic vessels, over which they

are immediately placed, but sometimes they are situated somewhat obliquely, towards the margin of the vessel, or they may even be as far distant as a semi-diameter of the vessel, in which case there is an oblique canal leading to the latter.

The openings (stomata) never exceed the size of an epithelial cell. The rich lymphatic plexus of the central tendon with these large stomata is obviously subservient to the absorption of the fluids of the peritoneal cavity, which, like the lymph, contains contractile cells, capable, from their size, of passing through the stomata. In the frog, which has no diaphragm, Schweigger-Seidel and Dogiel found that openings of a similar nature exist in that surface of the wall of the cisterna lymphatica magna that is turned towards the abdominal cavity. Dybskowsky also was able, by causing the absorption of coloured fluids from the pleural cavity of dogs into the lymphatic plexus of the pleura, to demonstrate the existence of similar openings between the epithelial cells. From these experiments we may now reasonably expect that analogous formations will be found in the pericardium and in the arachnoid membrane of the brain, and that, consequently, we may conclude all serous cavities to possess a very intimate connection with the lymphatic system.

Further, it has been shown, in regard to many epithelial layers, even in parts where the lymphatics certainly do not approximate the surface, that when they have been treated with nitrate of silver, sharply defined spaces exist between the epithelial cells which may be placed in the same category with the stomata above described. Oedmansson first described them in the epithelia of serous membranes. He drew attention to their occurrence in the epithelial stratum of the chyle vessels and of the follicles of Peyer; Ludwig, Schweigger-Seidel, and Dybskowsky demonstrated their presence in the pleura and peritoneum, and further showed that they were especially abundant in the small-celled epithelium which lies directly over the lymph vessels on the peritoneal surface of the central tendon of the diaphragm. They are distinguished from the proper stomata by their much smaller size, the largest only attaining the diameter of a red blood corpuscle, and they are principally found at the points of junction of several epithelial cells. I recognised these spaces when I first began to employ silver as

a means of staining the tissues; but have met with them under so many different conditions, that I am not at present satisfied of their nature. In perfectly fresh silvered preparations, preserved as carefully as possible in their natural condition, we frequently meet with areas of considerable extent in which scarcely any openings are present, whilst in others, again, they are very numerous; the difference being in no way attributable to the mode of preparation. At the same time, it cannot be denied that within a few hours after death, or as a consequence of mechanical violence, or careless preparation, they always appear more numerous, clearly on account of the epithelial cells becoming detached from each other. The variability in the appearances presented by perfectly fresh specimens may be explained on the supposition that at certain times, or under certain conditions, connected with the imbibition of fluids, the substratum of the epithelium opens, whilst under other conditions it closes up. At present no absolute proof has been adduced to show that they are really openings, nor has any one shown that solid particles can traverse them.

I must express myself in exactly the same terms in regard to the very regular and interesting appearances of a similar nature, situated for the most part at the points of junction of several epithelial cells, which are frequently exhibited in the lymph vessels of silvered preparations, but which are sometimes undiscoverable even when the greatest care has been taken in the preparation of the specimen. I endeavoured to obtain them constantly, and hoped, in accordance with what has been above stated, to accomplish this by permitting the central tendon to lie for several hours in diluted pericardial fluid, thus rendering its tissues as moist as possible with an indifferent fluid, yet without being able to observe the spaces occur with such constancy and regularity as, after the foregoing exposition and the observations I have still to make, was to be desired. The present condition of our knowledge may therefore be expressed in these terms, that stomata can be certainly proved to exist in certain lymphatic capillaries; that openings, at least of an occasional character, must also exist in other lymphatics, especially in absorbing membranes, though this still remains to be satisfactorily demonstrated, notwithstanding that

Oedmansson, His, and others have described foramina presenting features analogous to such stomata.

We come now to the essential point of the whole inquiry, the nature, namely, of *the relation borne by the lymphatics to the surrounding tissues.* And we must first ask whether definite channels exist by which the fluids transuded from the blood are conducted to the commencement of the lymphatics, or whether the surrounding tissues behave like Descemet's membrane, in which pores and canals are present of sufficient magnitude to enable them to be readily seen by means of the microscope? If we consider the phenomena of the absorption of fat, it appears absolutely requisite to assume, not only that there are foramina in the walls of the capillary lymphatics, but that there are channels in the surrounding substance of the parenchyma in the case of the villi, though in regard to the other rootlets of the lymphatic vessels, their existence appears less requisite, since their contents, apart from the lymph corpuscles which are probably formed in their interior, ordinarily consist of a fluid destitute of any undissolved particles, or oil drops. In the parenchyma of the villi, a plexiform disposition of the chyle constituents has been observed to be situated immediately beneath the epithelium, forcibly suggesting that special arrangements are here present, by means of which the vessels containing the chyle are brought into direct communication with the cavity of the intestine. Very recently it has been maintained by Letzerich that a special system of canals, commencing with cup-shaped organs, in the epithelium, conducts the chyle into the central lacteal; but, even in the event of this statement proving correct, there must still be apertures or canals analogous to those above described, which lead from the abdominal cavity to the lymphatic vessels of the central tendon of the diaphragm.

A lively discussion is still maintained, as to whether the lymphatics are closed channels, or whether they stand in communication with interspaces of the tissue, from which, indeed, they may be supposed to be developed. The former view has become more definite since Virchow and Donders advanced their doctrines respecting the stellate connective tissue corpuscles; the corpuscles, in consequence of the fusion of their membranes,

are supposed to form a continuous system of tubes, a plasmatic vascular system, or, as it was called by Kölliker, a system of serous tubules, easily suggesting what was said in precise terms by Leydig, that this system of tubules was intercalated between the blood capillaries on the one hand, and the lymphatic capillaries on the other, and constituted the direct path between them. This statement was mainly supported by observations made on the tail of the tadpole, in which Kölliker found a distribution of lymphatic vessels with dentated outlines in connection with stellate, angular bodies, the connective tissue corpuscles. Whilst all such stellate and angular bodies require the existence of a membrane to be admitted, both this plasmatic system and the lymphatic system were regarded as closed. Physiologists, however, and particularly Brücke and Ludwig, maintained the view that the roots of the lymphatics, themselves destitute of a membrane, commenced simply from the interstices of the tissues, or from the so-called lacunæ. Fohmann, and before him Mascagni, had already, by injecting the lymphatics with mercury, obtained, when sufficient pressure was employed, such complete injections as to arrive at the conclusion that the tissues were entirely composed of a close plexus of lymphatics, and that the solid tissues constituted only small trabeculæ and septa between them. Brücke, in support of this view, argues from the known fact "that when injections of the bloodvessels are performed shortly after death, and therefore whilst the fluids permeating the tissues, as the lymph and blood, still remain uncoagulated, in not a few cases either the entire mass of injection, or the fluid portion of it, returns by the lymphatic vessels, which thus become even more completely filled than can be effected after the employment of much care and trouble." Ludwig and Tomsa have, moreover, in their injections, driven gelatinous fluids into the ultimate lymph canals of the testes in man and in dogs, and the injection was found to fill almost all the intervals between the tubuli seminiferi, following their course, and thus occupying spaces which formed continuous lacuniform sheaths around the ducts. The contiguous lacunæ were divided from one another by very thin septa of connective tissue, in which the bloodvessels ran. On a small scale, therefore, the arrangements were similar to

those met with in the lymph sacs of Amphibia. The idea was consequently not far fetched, that these appearances originated from the manipulation of the specimen, and the extravasation of the fluid; and, in fact, this objection was raised by the opponents of the view held by Brücke and Ludwig; and Langer even pointed out that in the testes of the frog the lymphatic vessels do not form sheaths of this nature, but tubular plexuses, as is usual in the lymphatic capillaries of other parts. Nevertheless it cannot be doubted that in the testes of many Mammals the lymphatic tubes ultimately terminate in lacunar channels. Ludwig and Tomsa have further attempted to prove the existence of such interstitial lacunæ in other organs, as in the tongue and kidneys, and to demonstrate their connection with the lymphatic vessels.

From this exposition of the two opposite views it is obvious that they differ from one another in one point, which is deserving of especial notice. In the one view, the anastomosing connective tissue corpuscles form a plexus, the nodal points of which are represented by the body of each corpuscle; the fibres of the plexus are *hollow cylinders*, and their disposition, upon the whole, similar to that of the lymphatics. On the other view, the interstitial spaces depend for their form on that of the morphological elements of the tissues (ducts, fibres, etc.) between which they lie. They vary in their form and size, but in general, because by far the greater number of tissues consist of cylindrical or spherical elements with more or less convex surfaces, they constitute *fissures* (that is to say, spaces the transverse section of which is not circular, as in tubes, but elongated, presenting in some instances a very small, and in others a relatively large diameter). Special importance has been attached to this lacuniform character of the channels by Ludwig. At the point of transition of these into the proper lymphatics, the lymph path undergoes a sudden alteration of form.

In opposition to these two views, I have still a third to propose, which is in accordance with all the facts that have hitherto been observed. The essential feature of this is, that the masses of connective tissue, whether they form the exclusive structure of an organ, or are intercalated between the proper morphological elements of some other tissue, are tra-

versed by fine canals, the *serous canaliculi*, which are directly continuous with the lymphatic vessels. These canals, in many organs, form plexuses, so that portions of them appear to be branched in a stellate manner exactly resembling the connective tissue corpuscles. These last however, are not, as Virchow, Kölliker, and Leydig supposed, fused with the walls of the lymphatic vessels, but occupy the interior of the serous canaliculi, so that from this point they may extend into the lumen of the lymphatic vessels. Moreover, the serous canaliculi are not provided with a special wall, and are consequently not tubes, on which account they are to be distinguished from the serous canals of Kölliker, but are rather to be regarded as excavations in the remaining substance of the connective tissue. They do not, however, represent—and on this account my view is to be distinguished from that of Brücke and Ludwig—mere fissures between the specific components of the connective tissue, but are the interstices of the fibrous fasciculi and lamellæ of connective tissue, cemented to one another by a tenacious, homogeneous, firm material in which the serous canaliculi are buried. Their form and arrangement, whilst it is not independent of the form of the interstices, is yet not altogether identical with it, but peculiar, and one not entirely determined by the arrangement of the several morphological elements of the organ. On my view, therefore, it cannot be admitted that the commencement of the lymphatics are, as Ludwig imagines, simply lacunæ, whilst, on the other hand, it is equally opposed to the view that they constitute closed membranous tubes, as is maintained by the adherents of the doctrine that they owe their origin to the connective tissue corpuscles.

When organs composed of connective tissue, and recently removed from the body, are treated with solution of nitrate of silver, the solid parts alone become stained, whilst spaces and channels in the tissue remain uncoloured; the lymph and bloodvessels coming into sharp relief as colourless tracks. In the connective tissue itself, stellate, unstained figures make their appearance, which are consequently spaces, though not altogether empty, since, by this mode of treatment, connective tissue cells become dimly visible in their interior. His maintained that the silvered tracings of the cornea agree with the

form of the cells; in other words, that the solid substance presents cavities which precisely correspond to the cells and their processes. In the meanwhile, if we allow the corpuscles of the cornea, with all their processes, to come into strong relief, by exposure for several hours in the moist chamber (which is the best method of rendering them distinct), the ramifications of their processes are always found to be few in number, and the communications between their finest branches to be discovered only with difficulty, whilst the silvered lines form a close plexus; the stellate corpuscles of the cornea, however, do not become covered with the tracings. But further, we see the actively moving cells of the cornea traverse its substance in all directions, without, as a rule, attaching themselves to the processes of the stellate, immovable corneal corpuscles, though they sometimes do so with great distinctness; with the spaces in which the latter lie, channels must therefore still be in communication, which are not occupied by the protoplasm of the cells. Moreover, W. Engelmann, since the migrations take place in every possible direction, has drawn the conclusion that the cells run without obstruction between the fibrils of connective tissue, pressing in from one to the other; various circumstances, however, are in opposition to this view. By careful observation it may be seen that the movements of the migrating cells do not take place with equal facility in all directions. They become constricted at certain points, and these constrictions remain unaltered in position, whilst the several corpuscles force themselves through; again they appear to meet with an obstacle, and must pass round it, though the constricting and obstructing substance may be so delicate as not to be visible. But further, if the cornea, or other variety of connective tissue (independently of the cells) consists only of fibrils with intervening fluid, in cases where the injection of an insoluble mass has been effected by means of simple penetration, the whole tissue can be split up into fibrils, or, in the case of the cornea, into lamellæ, and we may then obtain the sub-cylindrical canals (Bowman's corneal tubes), which often form very distinct plexuses. It is true that the latter, as they appear after injection, present a very unnatural form, being dilated to an enormous extent, on which account, however, they

must not be at once cast aside as "artificial products," but they rather show, since their forms cannot be referred to the arrangement of the fibrils, that the interfibrillar and interlamellar substance does not possess, in all directions, an equal density, but must consist of a soft fluid mass, and a firmer and more resistant material. From microscopical investigation we learn that the corneal corpuscles are situated in the channels which contain the injection; this must consequently correspond with their natural position, and it follows that these spaces are, at least in certain directions, immensely dilatable, and can scarcely therefore possess a proper investing membrane. If we take all these facts into consideration, we must, I think, come unavoidably to the conclusion, first, that, in the denser organs composed of connective tissue, as the cornea, tendons, fasciæ, and cutis, the lacunæ between the fibres or fasciculi are not filled with fluid alone, but in great part contain a more solid cementing substance; and, secondly, that in this more solid substance there are no cavities constituting matrices for cells, although plexiform canals destitute of walls are present, which are partly filled with cells, and partly with a variable quantity of fluid consisting of the juice of the tissues.

Since the nitrate of silver, when properly applied, only colours the solid tissues, the serous canals appear as colourless bands, resembling the lymph and blood vessels, which can be followed to their finest branches with a facility proportionate to their breadth, or as they happen to be filled more strongly with fluid at the time when they were stained with the silver. We must attribute the incomplete appearance of the plexuses in some cases to the absence of fluid, especially where the wider parts only, in which the connective tissue corpuscles lie, make their appearance. The serous canals have, however, very different forms in the various organs. They appear as distinct plexuses of subcylindrical canals in the dense organs composed of connective tissue, to which reference has above been made, the form of the networks being in accordance with the stratification of the organ; so that in the tendons and fibrous organs the meshes are considerably elongated in the direction of the fibres, whilst in the cornea they are expanded into layers between the lamellæ, and are in communication with one another by comparatively few branches,

that perforate the lamellæ in an oblique direction. In soft interstitial and investing connective tissue, like the perimysium, the canals appear extraordinarily wide, the dilatations in particular being in close proximity with each other, and the solid tissue, in which the canals are imbedded, being much diminished in quantity. Lastly, in all soft organs lying immediately upon the surface, in the most superficial layers of the capsules of the joints, in the serous membranes, and in the mucous membrane of the intestine, the solid portions are reduced to thin septa, which very incompletely separate the closely approximated spaces lined with cells. All these varieties constitute gradations of one and the same type, the terminal members of which present, on the one hand, the form of a cylindrical tube, and on the other, that of a lacuna; neither of them, however, represent the typical form, and it is consequently most appropriate to employ the term canal, since it expresses nothing definite with regard to their form.

In opposition to the importance which I attribute to the silvered preparations, various objections have been adduced, with all of which I am acquainted, since I have myself formerly had to meet them; but from my numerous researches I draw the conclusion that all the indistinct appearances obtained by those who oppose my method, proceed from injuries, accidental rents, and alteration of chemical composition; and I still believe that no method is more suitable than mine. All objections to it may be disposed of in the words of Schweigger-Seidel: "The regularity of the figures, the constancy with which the same forms recur in certain localities, and the presence of nuclei, which however are not always equally distinct, in their interior, furnish satisfactory proof that they are not accidental formations." Schweigger-Seidel makes the above statement only in regard to the lines showing the presence of an epithelium, and maintains that the indications of the presence of serous canals, after the removal of the epithelium, originate in an albuminous layer, subjacent to the epithelium, and consequently upon the surface, and not in the interior of the connective-tissue lamina. I do not, however, quite comprehend why Schweigger-Seidel leaves quite out of consideration the markings produced by silver in the cornea; for in the cornea it is quite easy to demonstrate that the layer on which the silver acts is not equivalent to the anterior surface of the cornea, which first comes into contact with the solution of silver, but not unfrequently rather lies in close approxima-

tion to the membrane of Descemet. From the consideration of this one point, the doubt which he has expressed could be overthrown, and the proposition above advanced be also maintained in regard to the silvered markings of connective tissue.

The serous canals represent spaces which are continuous with the lymphatic vessels, and it may even be said that they

Fig. 58.

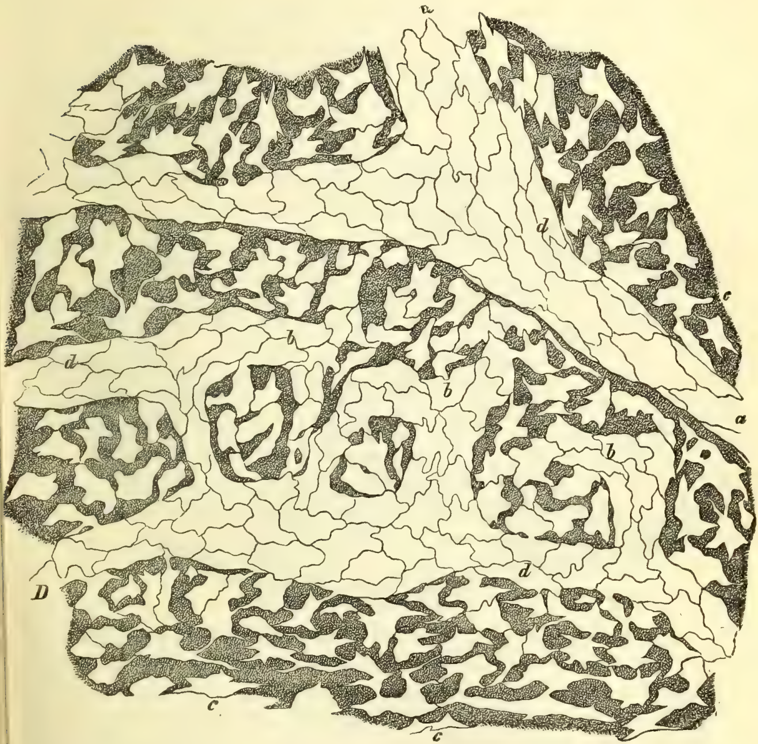

Fig. 58. Central tendon of the diaphragm of a Rabbit treated with silver. *a*, lymphatic capillaries with epithelium; *b*, commencement of the same; *c*, serous canals; *d*, transition of serous canals into lymphatic vessels most abundant at the border D. Magnified 300 diameters.

constitute the roots, so frequently sought after, of the lymphatics. As a proof of this, the following facts may be adduced: 1. In

silvered preparations, a direct transition of the colourless passages of the serous canals into the smaller lymphatics may be observed. Successful preparations of the central tendon of the diaphragm show in the most distinct manner the transition of the small cylindrical serous canals (see fig. 58) into the lymphatic capillaries. The latter, at their very commencement, frequently present dentated contours, and at the bottom of

Fig. 59.

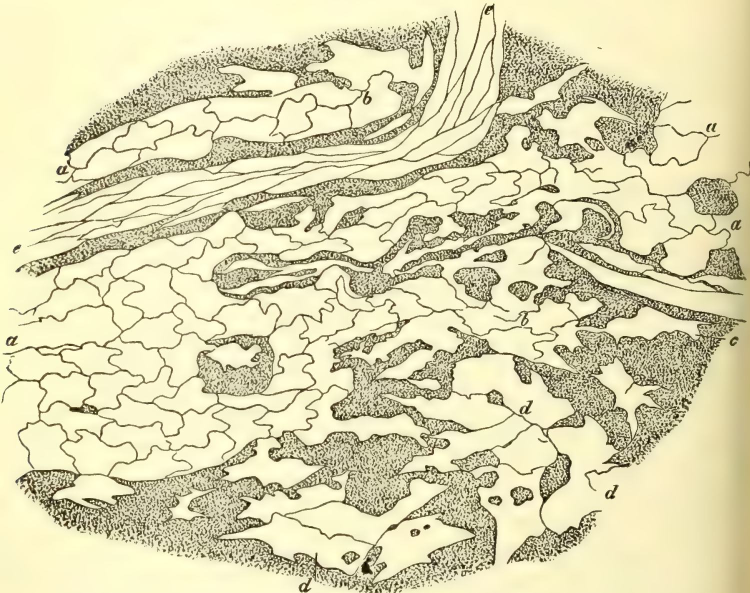

Fig. 59. Central tendon of the Rabbit, treated with solution of nitrate of silver, the most superficial serous layer immediately adjoining the pericardium being shown. *a*, lymphatic capillaries; *b*, their origin; *c*, serous canals with communications; *d*, serous canals equal in width to the origin of the lymphatic vessels; *e*, bloodvessel with epithelial cells. Magnified 300 diameters.

these depressions the limits of the lymphatic vessels very frequently become insensibly lost in the serous canal system. This disappearance of the boundaries of the lymph vessels it is very easy to understand is so much the more obvious in pro-

portion as the canal system is wider, and is consequently particularly well marked in the serous membranes and other analogous structures (fig. 59).

In preparations of this kind it is important to avoid everything that may produce alterations in the structures under examination; for if the contours of the lymphatic vessels and serous canals are in the smallest degree rendered indistinct and hazy, it is impossible to determine accurately the nature of their connection. But such blurred images are always obtained if the epithelium has not been carefully removed previous to the impregnation of the preparation with the solution of silver. His appears to have had only such indistinct specimens before him, as he believed that an unskilled observer might remain in doubt as to the continuity of the contours.*

2. If the lymphatic vessels be injected towards their rootlets, it is very easy, even with an insoluble injection, to produce extravasation into the tissue, by which it becomes more or less stained. Under the microscope we may then see in the softer tissues only a dense mass of colouring matter, without any of the ordinary canals being visible; harder tissues must consequently be selected, if we desire in this way to ascertain the path followed by the injection. In the fascia of the thigh of the frog, forming the wall of a lymph sac, I have succeeded in filling canals containing connective tissue cells with granular colouring material, by injecting the sac; and we may also force very fine injections through the lymphatic vessels of the cutis into the subcutaneous connective tissue, the fluid passing directly into channels that precisely agree in their form with the plexuses containing healthy pigment, *i.e.*, the ramifications of the so-called pigment cells; indeed, the injection may sometimes be propelled into the plexus of pigment cells itself. We cannot, therefore, entertain any doubt that the injection, if it escape from the capillary lymphatics, enters into channel-like spaces of the tissue, which are nothing else than the serous canals themselves, since they here contain the pigmented connective tissue cells. Moreover in all soft tissues, as, for instance, in the villi of the small intestine, plexuses first make their appearance; and then, when the injection has been driven with great force, the

* *Zeitschrift für wissenschaftliche Zoologie*, Band xiii., Heft. 3, 1863.

diffused tense infiltration is produced, in which no determinate figures are discoverable. Against these results it has been objected, and to a certain extent justly, that such appearances are due to over distension, and originate in extravasation or rupture of the tissues; and it is certain that they do not appear with the above-named injections, unless very considerable pressure has been applied. In the meanwhile, the injection of the substance of the villi occurs even when only very slight pressure has been employed; and we here possess a very good means of control by a comparison of the results obtained with the natural injection that takes place with the chyle. The same appearances are presented in both instances, of a plexiform arrangement of chyle drops around the central lacteal in the first instance, and ultimately of chylous infiltration of the whole parenchyma of the villus. Can it be possible that such a plexiform appearance of the chyle masses has given rise to the belief that the lacteals in the villi form a dense network still closer and more compact than that of the bloodvessels?

The open communication existing between the serous canals and the capillary lymphatic vessels enables the latter to receive substances from the former; and the facts that have already been adduced, in regard to the behaviour of the villi during chymification, afford sufficient evidence of the passage of a lymph current through the interstices of the tissues (serous canals) into the rootlets of the lymphatic vessels. Moreover, the passage of the cellular elements of the connective tissue from the serous canals into the lymphatics, although not as yet directly witnessed, is in the highest degree probable, since they migrate from place to place within the lumen of the former. Judging from silvered preparations, the communication between the rootlets of the lymphatic vessels and the serous canals is often so free as to render it difficult to determine the limits between them; this can, indeed, only be accomplished by determining the existence of an epithelium, and considering that the lymphatic vessels commence where the epithelium first makes its appearance.

The conclusions that have been here stated have by no means obtained general acceptance, and it must be acknowledged that further evidence is still required. We should endeavour to effect the physiologi-

cal impregnation of the tissues with insoluble colouring or other particles, and subsequently to stain them with silver, in order to establish the fact that the absorbed material passes from the serous canals into the lymphatic capillaries ; the evidence would be perfectly satisfactory, were it possible to propel the particles, whilst the preparation is under observation with the microscope, directly from the serous canals into the lymphatics. I, however, venture to hold that the theory as above stated affords an explanation of all the facts at present known, whilst others are not equally comprehensive. In order to render this evident, let us consider the facts on which the supporters of other views rely. Ludwig and Tomsa, for instance, regard the fissures they have discovered between the canaliculi of the testis as the origins of the lymphatic vessels, and they undoubtedly lie so close between the parenchyma,—not unfrequently investing the bloodvessels,—and the connective tissue is withal so small in quantity, that it is scarcely possible to look in this organ for other roots of the lymphatic vessels, that is, for a serous canal system. Ludwig and Zawarykin injected similar lacunæ in the kidneys surrounding the tubuli uriniferi. Tomsa made injections of the nose of the dog, and saw plexuses suddenly proceed from the injected capillaries, which he regarded as transverse sections of lacunæ intervening between the muscles, or fasciculi of connective tissue. At the same time, their fissure-like form was not demonstrated by him, and both his illustrations and descriptions agree equally well with my explanation, especially as it appears from them that fusiform cells (connective tissue corpuscles) are found at the borders of the injected canals. In the case of the kidneys, I have not been able to convince myself that the lacunæ in the tissue, serving as origins for the lymphatic vessels, are fissure-like in form. In regard to the lymph lacunæ of the testis, whether they exist to the extent described by Ludwig and Tomsa, or are less developed, they can afford no evidence on the mode of origin of lymphatics in other organs ; for His and Tommasi have demonstrated that they are lined by the characteristic epithelium of the lymphatic capillaries, and hence are most probably analogous to these rather than to serous canals. The other theory, which refers the rootlets of the lymphatic system to the connective tissue corpuscles, rests on a fact which is also in full accordance with my view ; namely, on the connection of the cells of the tissue with the dentated rootlets of the lymphatic vessels (Kölliker). I certainly do not participate in the doubts entertained by many respecting the lymphatic nature of these rootlets. It is true, indeed, that we cannot ordinarily perceive any current traversing them, since the fluid is as clear as water; but in one instance I was able, after pro-

tracted observation, to see a cell projecting from the terminal angular extremity of one of these rootlets gradually become absorbed into it; and which, in its brightness, its refractile power, and its size, completely corresponded with those tissue cells which are in contact with the lymphatic vessels; as it was entirely absorbed, it was immediately conducted, with moderate rapidity, but apparently passively, to one of the main trunks. I have not as yet been able to observe one of the stellate or fusiform connective tissue cells, which join with these lymphatic vessels, or lie quite on their exterior, to be pushed onward in a similar manner into the lumen of the vessel; yet I regard it as probable that this may sometimes occur. The above observation renders it more than probable that the tissue cells are not strongly adherent to the vascular wall, but lie in cavities which are continuous with the lumina of the lymphatic vessels. Large granular cells may also be seen in the interior of the larger-sized vessels of this description, lying near the wall, and at moderate distances from each other. These are considered by Kölliker to be collections of fat molecules constituting the remains of the primary formative cells; they usually present pale but well-defined outlines, possess numerous small teeth and projections on their surface, some of which enter the cavity of the vessel, whilst others penetrate the surrounding tissues. These cells do not give the impression that they are undergoing disintegration, but rather appear to me to be simply the connective tissue cells which hang from the interior of the larger vessels, and still remain attached to their walls. It might, indeed, be considered that these lymph passages or rootlets simply constitute expansions of the serous canals, leading to others by means of their closely proximated pointed processes, and an endeavour be thus made to prove that the serous canals and lymph passages are continuous. The question may be asked, do these persistent connective tissue cells under any circumstances develop into epithelial cells? I confess that I am unable to give a positive answer, and shall only here remark that, like Kölliker, I have been unable to obtain any evidence of the presence of an epithelial investment in these vessels by the action of nitrate of silver. After being injected with this fluid, the largest branches near the spine exhibited only confused lines which might be regarded as indications of an epithelium, whilst in the smaller vessels branched cells became coloured, around which were a number of fine lines resembling coiled fibres. Whether, as from this account appears probable, the peripherical portions of the lymph canals are destitute of an epithelium, or whether such an epithelium may yet be demonstrated by further investigations, all the peculiarities of these vessels agree in a most remarkable way with the

view of the origin of the lymphatic vessels from serous canals. It is not difficult, from these considerations, to obtain additional evidence in favour of my theory; nevertheless I do not venture to do so, since we are treating of peculiar and, so to speak, embryonal tissues of lymph capillaries that are, perhaps, as yet destitute of epithelium, and in a very early stage of development; connections and communications may therefore exist at this period, which at a later stage are in some way or other modified or altogether abolished.

If now we may consider the system of serous canals as the origin of the lymphatic capillaries, the former system of tubes appears to be adapted for the conduction of the proper fluids of the tissues, whilst the latter constitutes the collecting tubes which carry off the superfluous fluid. Regarded from this point of view the comparison of the structural character of the two systems is of great interest. Both are only sparingly present in the denser tissues that are permeated by only moderate quantities of nutritive fluid, as in the case of tendons; on the other hand, in tissues like the central tendon of the diaphragm and the mucous membrane of the intestine, in which the current of the nutritious fluid of the tissue is extraordinarily rapid, the lymphatic vessels are very abundant and wide in relation to the total sectional area of the serous canals; lastly, the serous canal system may have a great extension in relation to the entire efferent system of the lymph path, in which case the tissues are very soft and juicy, and the fluid in their interior undergoes only slow interchange, and is, perhaps, on this account, especially adapted to the formation of new cells. To the last category probably belong the looser masses of connective tissue which invest the several organs, and unite the interstitial connective tissue layers, on the one hand, with the serous and synovial membranes on the other. In point of fact, the outer layers of these tissues are very defective in continuity, whilst the serous canals are extraordinarily wide; the solid structures being only present in the form of thin membranes and trabeculæ, and we know from pathological processes how quickly a cellular infiltration occurs in them. In the tunica adventitia of the blood-vessels such cellular infiltrations have frequently been regarded as lymphatic vessels in a state of distension. In certain parts of the body this unusually wide serous canal system appears to

coalesce, and form larger cavities, which then become invested with an epithelium: of this the serous cavities may be taken as an example in a physiological point of view, and the so-called serous cysts in a pathological. Where spaces of this kind form in or upon the tunica adventitia of the blood-vessels, we obtain sheath-like investments resembling the lymph sheaths of the tubuli seminiferi. To these belong the *perivascular* lymphatics described by His as existing partly in the membrane, and partly in the substance of the brain and spinal cord; these are really interstitial spaces between the bloodvessels and the substance of the brain, continuous with a wide "epicerebral cavity" situated beneath the pia mater. That this last does not constitute a mere interstitial space may be maintained on the ground that it can be filled from the true lymphatic vessels of the pia mater. His has demonstrated the existence of an epithelium in the larger of these perivascular canals and sheaths, and they therefore represent the same grade of organization as the lymphatic capillaries. Macgillavry also found, in injected preparations of the liver, lymphatic sheaths around the bloodvessels, but it has not been satisfactorily ascertained whether they are or are not lined with an epithelium. Stricker has, moreover, described a similar arrangement of sheaths around the blood capillaries of the lower eyelid of the Frog; whilst Langer has shown that in this region only two lateral lymph tubes are present, which lie close to the bloodvessel, and occasionally unite by transverse anastomoses which cross the vessel like a bridge. It further appears from Langer's careful investigations in the Frog, where the large bloodvessels are ensheathed by lymph sacs, or by processes of the lymph sacs, that from the point of their entrance into the different organs an "invagination of the bloodvessels by the lymphatic tubes is no longer to be distinguished"; in the serous and mucous membranes two lymph vessels, but in the interior of the parenchymatous structures only a single lymphatic vessel accompanies each artery. These investigations afford an important caution against too hastily admitting the existence of lymphatic sheaths around the bloodvessels. Many authors were formerly inclined to ascribe a perivascular system of canals to the bloodvessels of other organs, or at least to seek for

lymphatic sheaths generally within the tunica adventitia of the bloodvessels. But this only is certain, that in the latter situation the serous canal system presents an extraordinary expansion, and is on this account predisposed to cellular infiltration.

The fluid contents of the serous canals, as well as of the lymphatic vessels, that is to say, the lymph itself, primarily comes from the blood; it is therefore a question of peculiar importance to determine what relation the serous canal system bears to the bloodvessels, and especially to the blood capillaries. At first sight it appears most natural to consider that the serous canals stand in the same communication with them as with the lymphatic capillaries. This was the relation which the authors of the last century understood by their vasa serosa, vessels which, on account of their small calibre, only permitted the passage of the colourless serum, and arrested that of the corpuscles. Leydig has translated this view into modern language, in stating that the connective tissue corpuscles are continuous not only with the lymphatic vessels but also with the bloodvessels. Führer, and before him Lessing, had already maintained the view that "the vasa serosa formed a plasmatic system connecting together the blood and lymphatic capillaries," in the interior of which the cells were situated. I formerly held it to be improbable that the serous canals were continuous with the bloodvessels, since I had not then given up the old view that the wall of the bloodvessels consists of a homogeneous substance. Since, however, it has been demonstrated by Aeby, Auerbach, and Eberth, by means of solutions of nitrate of silver, that the walls of the capillaries were composed of an epithelium, at all events in such organs as they had examined; since, moreover, the permeability of the vascular wall for the red blood corpuscles (Virchow, Stricker), and also for the colourless corpuscles (Cohnheim), has been noted under circumtances which, though certainly not normal, yet can nevertheless be so rapidly brought about that it is impossible to admit the occurrence of a qualitative change in the nature of the capillary wall, I consider it to be very possible that the serous canals may stand in the same open continuity with the bloodvessels as with the lymphatics. That such communications do actually exist under normal conditions is also rendered highly

probable by the well-known fact that in the lymph, and especially in the chyle, not only colourless, but also red corpuscles may be discovered. Herbst instituted a series of experiments in which he augmented the total volume of the blood by slowly introducing blood, in the greater number of instances, but frequently also other fluids, as milk, into the jugular vein ; and in these he constantly observed the presence of red blood corpuscles in the abundant contents of the thoracic duct, and, where that fluid was employed, milk corpuscles also. Lastly, Dr. Rud. Böhm has very recently seen in silvered preparations of the synovial membranes the serous canals become continuous with the blood capillaries in a manner very similar to that noted above as occurring in the lymphatic capillaries.

The Lymphatic Follicles.

In various parts of the digestive organs there are to be found, situated within the mucous and submucous tissues, and also in the spleen and the lymphatic glands either projecting from their surface or appearing on section, small spherical bodies of the size of a millet seed—the so-called Follicles (see the article devoted to the digestive tract and the spleen). From the description given by Brücke, it was already known that the solitary follicles of the intestine and of Peyer's patches stood in intimate relation to the vessels of the lymphatic system. And this has been fully borne out by the more accurate modes of investigation recently adopted, but it has been further proved that the lymphatic follicles of the pharynx, tonsils, and lingual glands are also much richer in lymphatics than the remaining portions of the mucous membrane ; that all these structures consist of tissues which recur in the lymphatic glands, and they may therefore truly be accounted a portion of the lymphatic apparatus. We must commence with the description of the follicles on this account also, that they represent a very simple type of the lymphatic gland.

The follicular tissue (adenoid substance of His, cytogenic tissue of Kölliker) is characterised, first, by its reticulum, and secondly, by the lymph corpuscle-like cells which are adherent to the reticulum.

THE RETICULUM, first demonstrated by Billroth, consists of very fine fibrils varying in their thickness, which for the most part pursue a straight course, and form a close network, the meshes of which are only sufficiently large to contain a few lymph corpuscles in each. The fibrils when fresh are extraordinarily pale, present a homogeneous appearance, and are distinguished from elastic fibres, to which, after the hardening of the gland, they present some similarity, by their lustre, and especially also by their chemical characters; acetic acid and soda making them swell up so strongly that they can no longer be perceived. The nodal points of this plexus are usually very small, and exhibit nuclei, but whether these are simply adherent to or are contained within peculiar cells occupying the interior of the substance of the fibrils remains to be ascertained.

The lymph corpuscle-like cells, which constitute by far the greatest part of the follicular tissue, become isolated with extraordinary facility. They are contained in the milky fluid which flows when sections are made, and differ in some respects, and especially in their size, from one another (see lymph). The fibrils of the reticulum, situated at the periphery of the follicle, are in direct connection with the intercellular substance of the surrounding connective tissue; they attach themselves also to the bloodvessels, and especially to the capillaries, which traverse the follicle in the form of a wide-meshed plexus. The vessels are thus supported by a framework of fibrils, and hang freely in the spaces of the meshes.

The relations of the lymphatic vessels are of special interest. It has been a subject of dispute whether the follicles are rich or poor in lymphatics; the presence of lymphatic vessels in the follicles has even been altogether denied, and the conclusion drawn that the follicles are of no special importance in the lymphatic system. It is true that lymphatic vessels are not present in the interior of each individual follicle; for even the most complete injection of the lymphatic vessels of the intestinal canal, as was pointed out by Teichmann, leaves the interior of the follicles free, whilst Frey's injections of the tonsils have shown that here also, however, abundantly lymphatics are distributed through the whole organ, none are present in the individual follicles. These injections have, however, shown

that the surface of each follicle is invested by an extraordinarily close network of lymphatic vessels, the several branches of which are widely separated from those of the neighbouring follicles. The results of the investigations of His and Recklinghausen have further shown, and the same thing may be recognised in the illustrations accompanying Teichmann's work, that it is common for the follicles of the intestine to be surrounded by a lymph lacuna, and for the lymphatic plexuses to have become so close that the several tubes coalesce with one another to form a single spheroidal fissure. These lacunæ or lymph sinuses (according to His) in some instances surround nearly the whole surface of the follicle, leaving only that extremity or pole uncovered which is directed towards the surface of the mucous membrane; the follicle therefore hangs freely in the lymph path, or in what we may consider as an enormously dilated portion of it. That we are here dealing with lymphatic lacunæ, analogous to the lymph sacs of the Amphibia, and not with simple interstices or spaces between the tissues, is obvious from the action of solutions of silver, which bring into view a distinct epithelium immediately continuous with that lining the efferent or larger tubes of the lymphatics.

The follicles of the digestive tract must therefore undoubtedly be regarded as belonging to the lymphatic system; they probably form lymph cells in their interior, which pass into the lymph lacunæ, and then constitute ordinary lymph corpuscles. The relations of the epithelium investing the follicle on the surface directed towards the lymph lacuna, and the presence or absence of persistent openings for the passage of lymph corpuscles, are points that still remain to be elucidated.

Relations to the lymphatic system, of so intimate a nature as this, have, up to the present time, only been demonstrated in the above-mentioned follicles, whilst really nothing is known respecting the lymphatics of the well-known Malpighian corpuscles of the spleen, though they otherwise agree in structure with the follicles of the intestine; and we are equally ignorant of the lymphatics of the rest of the splenic tissue. The relations of the Thymus, again, which essentially consists of follicular tissue, to the lymphatic vessels, has also not hitherto been demonstrated.

Lastly, there are also found in certain organs composed of connective tissue, as the peritoneum and pleura of Mammals, and the mesentery and urinary bladder of the Frog, such large accumulations of lymph corpuscle-like cells in the interior of very vascular regions, as to cause them to present the greatest similarity to the follicular tissues, though here, again, no intimate relation to the lymphatic vessels is capable of being demonstrated. It is noticeable, however, that, in regard to the chief division of the bloodvessels, these structures differ from those of the lymphatic follicles proper; for whilst in the latter the main trunks are distributed upon the surface, the artery occupies a central position in each follicle of the spleen, so that these appear to represent a dilatation of the tunica adventitia: on the other hand, veins are altogether absent in the interior of the splenic follicles. All these differences in the arrangements of the vascular system are, however, insufficient to justify us in attributing to these structures a function different from that of the lymphatic follicles of the digestive tract; they, too, probably constitute centres of development for the lymphatic cells which are carried away from the splenic follicles, not indeed by the agency of lymphatic vessels, but by other passages, as by the veins which form a very dense investing plexus around them (Basler), and by the analogous structures of the serous membranes consequent upon their communication with the above-described cavities.

The Lymph Glands, Glandulæ Lymphaticæ.

Up to a very recent period, the structure of the lymphatic glands was classed with those in which no efferent duct could be discovered. The lymphatic vessels were seen to penetrate the surface of the gland at numerous points, as the vasa afferentia, and to emerge from the hilus of the gland as vasa efferentia; but in the interior of these organs the lymph path, especially in its relation to the glandular structure, was in the highest degree obscure. His, in the first instance, and subsequently Frey and Teichmann, have furnished intelligible accounts of their structure; and although their descriptions certainly differ in some few points, it nevertheless appears to me

that these differences are of a subordinate nature, and that we may now consider a perfectly clear description can be given of all the structural arrangements presented by these glands.

The lymphatic glands exhibit, not only in different species of animals, but also in one and the same individual, a varying structure which is undoubtedly difficult to define; the first examination of preparations of the lymphatic glands produces a very confused impression, as may best be understood if it be borne in mind that the variability which in general characterises the lymphatic system manifests itself especially in the structure of these organs. The lymph paths in particular exhibit the greatest variations in form, sometimes being tubular and at others fissure-like or lacuniform, both constantly and for the most part very suddenly passing into each other.

In the larger and generally also in the smaller lymphatic glands, two substances are distinguishable (Fig. 60), which may be designated the *cortical* (A), and *medullary* (B).

It is true that these names cannot be taken in a strict sense, since if the medullary substance be regarded as occupying a central position surrounded by the cortical substance, we not unfrequently find, on the contrary, considerable portions presenting themselves at the surface of the glands, and this elsewhere than at the bottom of the depression which represents the so-called hilus of the gland, and is occupied with connective tissue, the tissue of the hilus. In the subcutaneous lymphatic glands of the dog, for example, the medullary substance constantly appears at the surface, forming spots which may be easily recognised with the naked eye by their white colour, and are frequently separated from the remaining portions of the gland by a yellowish pigmentary border. In these glands no true hilus is present. It cannot be maintained that a sharp distinction exists between the two substances, and we shall hereafter see that there is no essential difference of structure; but that the follicles of the cortex, which are usually regarded as characteristic of it, find their complete analogy in the medullary substance.

Nevertheless it is advantageous, in the first instance, to distinguish between the two substances, since in many animals the difference between them is even macroscopically very per-

ceptible, as in the ox and horse, in both of which the medullary substance presents an intensely brown colour. The finer points of structure are best defined and most clearly visible in the ox, and it was therefore very fortunate that His chose the glands of this animal for his investigations. If sections be made from fresh glands, especially with high powers, we usually see only a homogeneous tissue, in which small lymph cor-

Fig. 60.

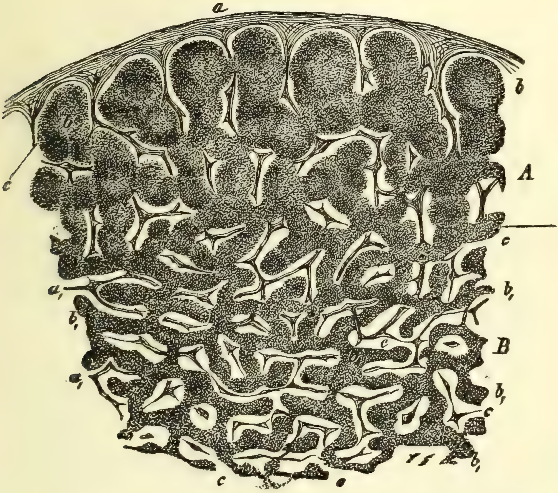

Fig. 60. Vertical section of a lymphatic gland from the Ox. A, cortical substance; B, medullary substance. *a*, capsule; *a′*, trabeculæ; *b*, follicles; *b′*, follicular cords (medullary cords); *c*, lymph path, designated in the follicles lymph sinus or investing sinus; the fine fibres traversing this are omitted. Preparation macerated in alcohol, and magnified 25 diameters.

puscles, and indeed successive layers of cells, are arranged so closely that an intermediate substance is only apparent at the very thinnest parts of the sections. For the purpose of demonstrating the different structures, it is expedient in the first instance to harden the glands; and this can best be accomplished by maceration in alcohol, after which extremely fine sections must be washed, or still better, gently pencilled out. When this has been done, sections of the medullary substance are found to present a dotted character; these, however, are

not complete perforations, but are distinguished from the denser tissue in consequence of their much greater transparency, and also by the circumstance that they contain the pigment, and this in the most marked manner in the ox; with still higher powers (see fig. 61), we see that they are traversed by fine fibres which are frequently arranged in a stellate manner, and often contain nuclei or cells to which granular masses of pigment cleave.

Fig. 61.

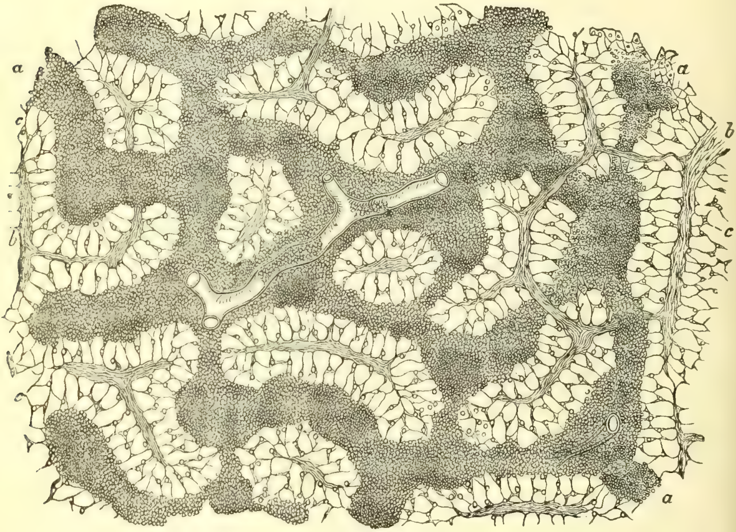

Fig. 61. Section of the medullary substance of a lymphatic gland from the Ox. *a*, follicular cords; *b*, trabeculæ; *c*, lymph path. Magnified 120 diameters.

These fibrils unite to form thicker fasciculi of connective tissue, *the trabeculæ,* which are not unfrequently flattened; they lie always in the centre of the above-mentioned spaces, and constitute the main trunk from the sides of which the fine fibrils of the reticulum are frequently given off nearly at right angles; the latter are then attached on the other side to the cords of the compact substance (*medullary cords* of Kölliker; *medullary tubes* of His; *lymph tubes* of Frey).

These medullary cords (fig. 61) have the same structure as the tissue of the lymphatic follicles (see above), consisting

consequently of a reticulum of fibres enclosing lymph corpuscle-like cells, and may correctly be termed follicular structures, or *follicular cords.* The reticulum is distinguished from the fibrous tissue of the light spaces by the circumstance that the fibrils are individually finer, and the meshes of the plexus, especially in the peripheric layers, are much smaller.

For their most remarkable peculiarity—namely, their want of transparency, as compared with the light spots—the follicular cords are indebted to the large number of these cells. It must be admitted, however, that this most obvious difference between the cords and the lighter spots is but slightly marked in fine sections of the recent or in thicker sections of the hardened gland substance, before they have been brushed and washed, since in the latter also the lighter spaces are fully occupied with lymph corpuscles. And, on the other hand, the differences may again disappear if the brush has been too freely used, since then the reticulum alone remains in the follicular cords. From this it follows that the lymph corpuscles are by some means firmly retained by the latter, whilst in the more transparent portions of the lymph path they lie loose and unattached. It may be asked, how are the corpuscles fixed in the reticulum of the follicular cords? It is probably effected by the great compactness of the reticulum and the smallness of its meshes which retain any lymph corpuscles that are traversing it either by a natural or artificial current, and it is also possible that the lymph cells adhere more loosely to the trabeculæ since they only touch by a few points of their surface.

The mode of fixation of the lymph corpuscles is a matter of considerable importance. If, by plunging the point of an injection syringe into its tissue, we propel various solutions through the substance of a lymphatic gland, or inject the organ through its afferent vessels, we shall find that we are able to clear the more transparent parts of corpuscles as effectually as by brushing, whilst the follicular cords preserve their cellular contents almost intact. Only a very small amount of pressure is required to accomplish this—no more, in fact, than that at which the lymph current ordinarily traverses the gland. It may be fairly maintained, therefore, that the natural lymph current is powerful enough to wash away the lymph corpuscles

contained in the light spaces; and we may further draw the conclusion that each separate lymph corpuscle only temporarily occupies this tissue. In other words, these light spaces only constitute a path by which the corpuscles can be conducted away, whilst the reticulum of the follicular cords constitutes their proper domicile.

Injections of the lymph and blood vessels of the lymphatic glands furnish evidence, however, of still other and more important differences between the lighter spots and the follicular cords (see fig. 62). The distribution of the bloodvessels, properly speaking, only occurs in the latter; they alone contain capillary networks, whilst the lighter spaces contain only the larger bloodvessels, which, proceeding from the trabeculæ, traverse them in order to reach the follicular cords. On the other hand, injections, whether made by puncture of the gland substance or through the afferent ducts, prove to us that the light spaces represent the true paths pursued by the lymph. They, for the most part, fill with great facility, and the injecting fluid, if composed of thick solutions of gelatine and some coarsely granular colouring material, remains confined and limited to their interior. If, however, the fluid is more watery, and the colouring material very finely divided, it penetrates into the follicular tissue, in all instances clearly entering from the periphery. In cases where a very tense natural injection of the mesenteric glands has occurred with chyle, it is easy to demonstrate the presence of chyle granules in the peripheric portions of the follicular tissue; from whence it follows that the follicular cords are not completely excluded from the lymph path. Thus it appears that although the reticulum is very compact near their surface, it will still permit solid corpuscles to penetrate from the lymph path into the interior of the follicle, and therefore conversely it is probable that material particles—lymph cells, for example—may pass from them into the lymph path.

We are thus able to differentiate three separate parts in the tissue of the lymphatic glands: (1) the follicular tissue; (2) the trabeculæ; and (3) the lymph path. And we must now follow the form and arrangement of these into further detail. The trabeculæ are direct processes from the sheath of the lymphatic glands (see fig. 60), and, like this, consist of connective tissue,

together with, in many animals—as the horse, sheep, and ox—a considerable quantity of smooth muscular fibre (O. Heyfelder). The processes which the sheaths give off towards the interior of the lymphatic glands are at first flat septa, which, near the centre, break up into cylindrical or subcylindrical cords, the trabeculæ, which ultimately become continuous with the con-

Fig. 62.

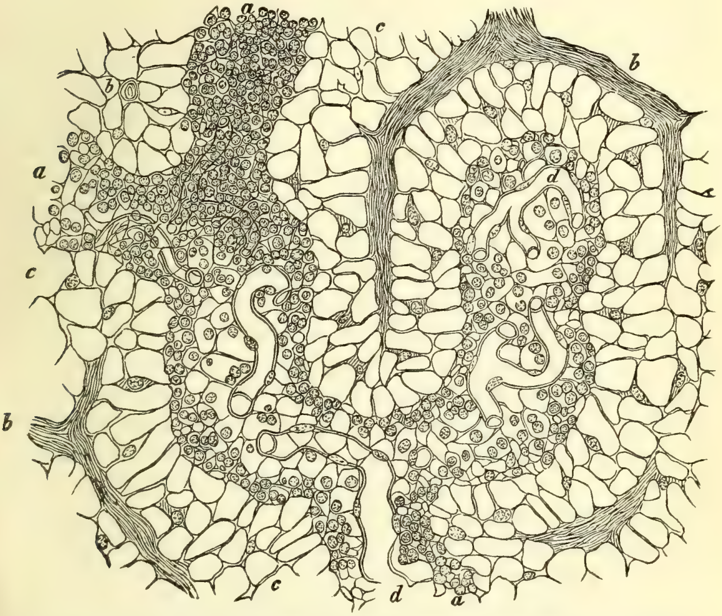

Fig. 62. Section of the medullary substance of a lymphatic gland from the Ox. *a*, follicular cord; *b*, trabeculæ; *c*, path pursued by the lymph; *d*, bloodvessels. Magnified 300 diameters.

nective tissue of the hilus. At the surface of the gland the trabeculæ are situated at a distance from one another, and usually, in conjunction with the external sheath, enclose alveolar-like spaces, in such a way that the latter are only uninvested on the part looking towards the hilus. As they divide into rounded cords, the trabeculæ come into much closer approximation; the spaces which they invest are consequently smaller than the alveoli, and at the same time are in much more

free communication with each other. The follicular tissue, as a general rule, forms rounded cord-like masses, connected with one another in a plexiform manner; these are not usually perfectly cylindrical, but present projections, and are sometimes even quite moniliform. Near the surface of the lymphatic glands the follicular cords give off particularly well-marked dilatations of perfectly globular form, constituting the granules that, both on the surface and also on section, are clearly perceptible to the naked eye, and are commonly described as follicles. The cortically situated follicles of the lymphatic glands are thus nothing but the club-shaped dilatations of the follicular cords of the medullary substance, and may be the more easily identified with the latter, since not unfrequently large globular follicles are to be found deeply situated in the medullary substance. The follicular framework is so intercalated in the meshes of the trabecular system, that the superficies of the follicular tissue never comes into immediate contact with the superficies of the trabeculæ, and the spaces which intervene between the two are the lymph paths. The form of the latter consequently agrees with the form of the two above-mentioned tissues, so that at the superficies of the alveolar trunks they present an approximation to the form of concave spherical shells (lymph sinuses, His; investing spaces, Frey); whilst in the interior of the gland they simply assume the form of the spaces left by the trabeculæ of the follicular network. It is easy to demonstrate, from injected preparations, that the vasa afferentia, which, as is well known, are distributed on the surface of the gland, directly open into these concave areas, or lymph sinuses, and thus suddenly become converted from cylindrical tubes into lacuniform spaces. With injections of solutions of silver it is particularly easy to recognise the immediate transition from one to the other, on account of the facility with which the epithelium of the afferent lymphatic vessels can be followed on the outer wall of the lymph sinus. It is, however, unquestionably a matter of greater difficulty to establish the origin of the roots of the vasa efferentia from the internal lymph paths. This is not in any measure due to any difficulty of filling the vasa efferentia with injection in the direction of the current. On the con-

trary, if the injection is sufficiently fluid, this may be accomplished with extraordinary facility, especially when the mode of injection by puncture is adopted. In such cases it will be found that the vessels of origin of the vasa efferentia have such a remarkably moniliform character, and communicate so frequently with one another, that they form quite a cavernous structure. The several canals in this cavernous plexus are so short that their union with the lymph paths of the medullary substance are far more difficult to recognise than if they were continuous with a few elongated canals. A general view of the relations existing in these parts may be best obtained from injections with solutions of silver (see fig. 63), and from these it can be established that the branches of the plexus, which up to this point have presented an approximatively circular section, suddenly undergo enormous dilatation, and into the lumen of these dilatations the several segments of the medullary substance imbedded in the hilus substance project, whilst the connective tissue walls of the cavernous plexus become continuous with the trabeculæ of the medullary substance. The indications of an epithelium may be easily traced from the lymphatic tubes to the trabeculæ, and may further be followed on them through the medullary substance. But the trabeculæ and septa at the periphery of the glands exhibit also, in silvered preparations, the same characteristic indications of an epithelium; and I have so frequently been able to satisfy myself of the presence of this, that I may venture to say that they are invested by an epithelium throughout the whole gland. The characters of the lymph path at its entrance into and at its exit from the gland are essentially similar. The relations of the several parts may be most simply represented by considering a rete mirabile to be introduced between them, the several branches of which suddenly diverge from the extremity of the afferent vessel, and then proceed to divide and subdivide, becoming consequently more attenuated. These finer branches perforate the intervening layers of tissue in all directions, freely anastomosing with one another, and finally suddenly reunite in the extremity of the continuous and tubular efferent vessel. The follicular substance is chiefly developed in the dilatations near the point at which the vasa efferentia

are attached, and from this point becomes gradually more and more attenuated, till it loses itself on the lymph path at the borders of the medullary substance.

This schematic representation of the arrangement of the lymph path corresponds to a fact of no small importance. Teichmann has shown that at certain points, in man especially, near the knee, retia mirabilia frequently occur in the place of

Fig. 63.

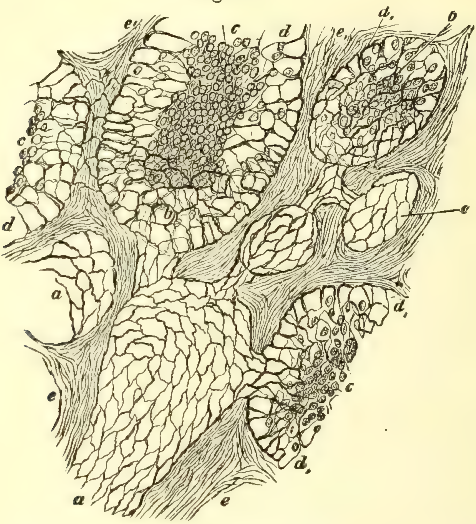

Fig. 63. Section from the medullary substance of a mesenteric gland of a Dog, after injection with silver. *a*, rootlets of the vas efferens, with a lining of epithelium in their interior ; *b*, dilatations of the channels, also lined by epithelium, and containing in their interior some gland substance with a follicular cord *c* ; *d*, fibrils traversing the lymph path, upon which, again, as at *d′*, an epithelium may be distinguished; *e*, fibrous intervening substance, which at *e′* forms trabeculæ. Magnified 200 diameters.

true lymphatic glands, differing from the latter in the circumstance that the lumen of the several branches is clear and free from follicular tissue. Teichmann maintains that the lymphatic glands originate from these by accumulations of lymph corpuscles, which attach themselves to the interior of the vessels, and here form knots or clumps composed of follicular tissue.

This view of the mode of origin of the lymphatic glands, which is similar to that formerly proposed by Engel and others, agrees but little with the recent observations of Sertoli, who found that lymph canals lined with epithelium first made their appearance; around these the connective tissue increased; and in this, and consequently *external* to the original lymph path, accumulations of cells occurred to form the follicular glandular substance.

The structural arrangements here described as existing in the lymphatic glands can be most easily recognised in the glands of the ox and sheep. The glands of other mammals, and of man, present difficulties which are easily set aside if the fundamental structure of the lymphatic glands, as we now understand it, proves to be correct. In the lymphatic glands of oxen, the lymph path and follicular tissue may be distinguished with precision, (1) because the fibrous framework of the lymph path is beset with pigment both in the medullary and the cortical substance, whilst the follicular tissue is colourless; (2) because the follicular tissue through the entire medullary substance forms continuous uninterrupted cords, which for the most part exceed the lymph paths in breadth. In the lymphatic glands of man and the dog the relations of the medullary tissue are somewhat different, the lymph path here occupying relatively a much greater space than the follicular substance. Moreover, the trabecular system is much less completely developed, and it is not every section of the lymph path which, as in the lymph glands of the ox, is traversed throughout its whole length by a trabecula; for sometimes the position of the trabecula is not distinguishable, so that between two neighbouring follicular cords there appears only a homogeneous framework of fibrils; whilst sometimes closer plexuses are formed by these fibres, which present nodal points analogous to the trabeculæ. Lastly, the follicular cords, especially in the lymphatic glands of man, present less sharply defined surfaces towards the lymph path than in the ox, the reticulum is of looser structure, and the lymph corpuscles adhere less firmly; and thus, by the too firm use of the brush, appearances are easily obtained, of which it is much more difficult to give a satisfactory explanation than in preparations obtained from the ox. Lastly, it is to be remarked that the proper lymph tubes penetrate far deeper into the medullary substance. The lymphatic glands of man and the dog, again, differ essentially *inter se* in this point, that in man a highly developed hilus substance is present, giving a correspondingly distinct reniform shape to the glands, and only absent or sparingly developed

in those of the mesentery, whilst it is usually altogether absent in the lymphatic glands of the dog, whilst the medullary substance and the efferent vessels, as already mentioned, are much more visible upon the surface. The lymphatic glands of the pig exhibit peculiarities of quite an opposite character; here the follicular structure preponderates in extent over the lymph path, and nodal dilatations appear throughout the entire medullary substance on the follicular cords; that is to say, true follicles are formed, which make their appearance on section when examined with the naked eye, and the lymph path is so narrow that its injection can only here be effected with the greatest difficulty. According to Franz Schmidt, in other parts of the body of the pig, as in the pharynx, exceedingly strongly developed follicles are found; but it requires still further investigation to determine whether this is a consequence of the fattening of these animals, as Schmidt thinks, or whether it results from some peculiarity of this genus.

A more exact investigation is still required in order to determine the relations of the epithelia to the several tissues of the lymphatic glands. I have been unable to discover any epithelial layer on the follicular cords. The mode of connection of the fibrous framework with the epithelium is of special interest. I have frequently distinctly seen that epithelial cells are continued from the surface of the trabeculæ upon the thicker fibrils (see fig. 63, *d*); these consequently possess an epithelial investment of the same kind as the nerves which traverse the lymph sacs of the frog. It still remains to be ascertained whether this relation is generally present or is only partial, and whether the follicular cords, as has hitherto appeared to me, are destitute of epithelial cells, and thus lie naked in the lymph path.

The CHYLE, or milk-white fluid formed during digestion, and contained in the lymphatics of the intestine, and the LYMPH, which is the colourless, slightly opalescent fluid contained in the remaining portions of the lymphatic system, coagulate like the blood, and then separate into an albuminous serum, and a clot, which last contains the morphological elements—the lymph corpuscles or cells. In addition to these there are found, though in very variable proportion, small granules of rather high refractive index, which were formerly termed elementary granules, and are in all probability minute drops of oil. In the chyle there are also extremely small points likewise consisting of oil, and termed the molecular base of the chyle; these are present in such enormous numbers as to

impart to the chyle its opacity and dense white appearance; lastly, there are red blood corpuscles. The lymph corpuscles are now universally admitted to be identical in all their characters with the colourless corpuscles of the blood. They show in particular the same constantly varying form and the same phenomena of contractility, as long as they are living; whilst they assume the spheroidal form, which was formerly considered to be their natural shape, as soon as they die. The manipulations that up to a recent period were adopted for microscopical examination very easily kill them, and thus a fatal effect is produced by evaporation, by the addition of water, or of saline solutions containing more than 2 per cent. of salt. Even mechanical agencies, as the weight of the covering glass, are sufficient to rapidly extinguish all indications of life. Whilst the substance of the lymph cells during life is highly refractile, and even possesses a peculiar brilliancy, it becomes paler and dull after death; coincidently there appear small points (perhaps fat drops) in its interior, and in their centre a nucleus which is usually strongly granular. The corpuscles of the lymph, like the colourless corpuscles of the blood, are not all exactly alike; thus there are some which present a granular character, whilst others present the form of very large cells with multiple nuclei, and others, again, are very small, and were formerly not recognised as true cells, but were described as free nuclei. Undoubtedly in the latter by far the greatest part of the body is occupied by the nucleus, so that this is often only invested by an extremely thin layer of extraordinarily pale cell substance, which very easily undergoes disintegration. Lastly, we also sometimes find in Mammals and Amphibia large lymph corpuscles with brown granules in their interior, thus constituting pigment cells. In the various sections of the lymphatic vascular system the quantity of these elements varies, and they especially differ in their number according to whether the organs from which the lymph vessels proceed are in a state of rest or activity.

From whence now do these various morphological elements flow? Where is their place of origin? Formerly it was believed that they only originated in the lymph path, and the elementary granules were regarded as representing the very commence-

ment of organization; and even within a very recent period it has been sought to establish the view that the lymph follicles and the lymphatic glands are the only seats of origin of the lymph corpuscles, and that these continue to increase by fission after their entrance into the lymph path; but such processes of division have not been observed in any trustworthy manner, and I have only once had an opportunity of directly observing under the microscope how out of a lymph cell a young lymph corpuscle situated near the nucleus was suddenly ejected; I was not, however, able to ascertain how it originated. The formation of lymph cells in the follicles of the lymphatic glands, on the other hand, can at least indirectly be demonstrated; for the lymph which is carried by the vasa efferentia from the glands is always far richer in cells than that which is flowing towards them, and moreover the lymphatic vessels which come from the intestinal follicles, and especially from the Peyer's patches, furnish a lymph containing a far greater number of cells than the rest of the lacteals (Kölliker). The follicular substance of the lymphatic glands is probably to be regarded as the chief formative centre for the lymph cells; it would, however, be going too far to say that the lymph corpuscles proceed exclusively from the lymphatic glands. The very precise observations of Herbst and Teichmann show that cells are already contained in the lymph of man and mammals before it has traversed the lymphatic glands. In all probability such corpuscles proceed from the connective tissue in which the lymphatic capillaries are distributed, and in the form of contractile connective tissue corpuscles may easily have migrated from the serous canals into these capillaries. It is impossible to ascribe the office of the formation of lymph corpuscles exclusively to the follicular apparatus, or even to the lymphatic glands, because, so far as we at present know, true lymphatic glands are absent in the Amphibia, notwithstanding the abundance of cells in their lymph.

According to this, the question of the arrival of the lymph corpuscles in the peripheric plexuses of the lymphatics is connected with the question of the origin of the migrating connective tissue cells. In obtaining a reply to these inquiries, the researches very recently made by Cohnheim, and subse-

quently by F. A. Hoffmann, under my direction, in regard to the genesis of the pus corpuscles, are of great importance, since the characters of the latter agree in all respects with the lymph corpuscles, migrating connective tissue corpuscles, and colourless blood corpuscles. Insoluble colouring matters are, it is well known, rapidly absorbed by all these contractile cells when brought into contact with them. If, now, some such colouring matter, capable of being easily recognised (for which purpose vermilion is best adapted), be introduced into the bloodvessels of a living animal, the colourless corpuscles take up the particles into their interior; if, at the same time, an inflammatory process be excited in some organ, as in the cornea, pus corpuscles containing this colouring matter may be met with in the inflamed connective tissue, and even in the healthy cornea, but it is especially in the loose interstitial connective tissue that some migrating corpuscles containing the pigment may be discovered. We can only draw the conclusion from this, that such corpuscles must have been sufficiently approximated to the circulating blood to be able to withdraw the pigment from the blood. The simplest view is that they have entered in the blood itself, and thus, previous to their migration into the tissues, were colourless blood corpuscles. On this ground Cohnheim is opposed to the theory of Virchow, according to which the pus corpuscles originate in the connective tissue itself, and maintains that pus corpuscles are nothing but vagrant colourless corpuscles, and consequently are formed in those organs to which we refer the origin of the latter; that is to say, in the spleen and lymphatic glands. The immediate consequence of this doctrine is that the healthy migrating connective tissue corpuscles, as well as the lymph corpuscles of the peripheric lymphatics, must be brought to the tissues with the blood, and that both originate in the spleen and lymphatic glands; the latter, however, in the circuit of the blood through them, would certainly furnish similar cells to those which are brought to them in the vasa afferentia, which would also pass out by the vasa efferentia. There are still some additional grounds of support to be adduced for this doctrine of the migration of the colourless blood corpuscles. Cohnheim in particular rests upon direct observation of the first stages of

inflammation in the exposed mesentery of the frog, where he saw the colourless corpuscles, which, as usual whenever the blood current is retarded, accumulate in the lateral quiescent layer, and traverse the vascular walls, especially those of the veins, in order to migrate in the well-known mode; and thus the observation formerly made by Waller* in 1846, but again forgotten, except in England, under the predominant influence of Virchow's teaching, has reassumed its proper position. Hering has moreover observed in the mesentery, when spread out under the microscope, that the escaped colourless blood corpuscles enter into the lymphatic vessels ensheathing the blood-vessels, in order to be transported to other parts as lymph corpuscles. On these grounds we shall certainly be inclined to regard this doctrine as well founded; nevertheless, in spite of considerable attention to this question, I have been unable to arrive at any very positive conclusion, and cannot avoid making a few observations. In the first place it is certainly not easy to follow a particular corpuscle through its whole course from the blood current through the venous wall into the surrounding tissue, or to exclude the suspicion that the escaped cells proceed, not from the vascular wall, but from the adjoining connective tissue layers; secondly, the migration does not occur immediately after the exposure of the mesentery, but only after the lapse of some hours, when the most serious retardations and disturbances of the circulation have occurred. It is true I have been able to observe the migration of colourless blood corpuscles under much more favourable circumstances, and without remarkable alterations of the blood current, in the tail of narcotised tadpoles, not only in the capillaries, but in the small veins and arteries, and on these grounds I should not object to accept the doctrine that the migrating cells of the connective tissue proceed from the blood current, were it not that, (1) in consequence of the narcotisation, a certain retardation of the circulation was present; (2) that it was embryonal tissue that was under examination; and (3) that other observations are adducible, admonishing us that, with such movable elements, and structures so disposed to wander, we must exercise extreme

* S. Kosinski, *Wiener Med. Wochenschrift*, 1868, Nos. 56 and 57.

caution. I have especially observed that not only colourless cells escape from the blood path, but that migrating corpuscles of the connective tissue penetrate into its interior. After their entrance they creep along with long processes applied to the wall, in order again to escape at another point. What should we say if, in the above observations upon the mesentery, the escaping cells prove to be only such penetrating cells, which have entered either at a neighbouring point of the vascular wall (either of a vein or a capillary), or perhaps have crept on to a more distant point in the arteries, or have originally been formed in the surrounding tissue ?

Whether the lymph corpuscles and the migrating connective tissue cells originate in the place where they are met with, and become converted into immovable connective tissue corpuscles, as I have already stated is not impossible, or whether they are brought to the tissues from some distant point in the blood current, the above experiments so far afford evidence that they must move in spaces which stand in direct communication with the interior of the bloodvessels. The larger the quantity of vermilion that is introduced into the blood current, so much the more abundant are the corpuscles containing pigment discoverable in the lymph sacs of the frog. Hering found that in narcotisation with opium lasting for some hours, the lymph vessels of the liver became extraordinarily rich in lymph corpuscles, together with red corpuscles; and Toldt observed that if insoluble anilin was simultaneously introduced into the blood current, the lymph paths in the medullary substance of the lymphatic glands of the liver became tightly packed with blue-tinted cells (admittedly without the presence of free pigment granules), between which were heaps of red blood corpuscles. The red blood corpuscles constantly present in the lymph, and especially abundant in the chyle, were sometimes formerly regarded as being developed in the lymph path from lymph corpuscles, but more recently they have been considered to enter the lymph path by rupture of the vessels. According to still more recent experiments, however, showing the permeability of the walls of the bloodvessels (see the section on the bloodvessels), and the connection of the blood capillaries with the serous canals, the presence of red blood

corpuscles is no longer remarkable. The serous exudations found in the larger cavities of the body exhibit in all their characters, in their capability of coagulation, as well as in the number and nature of their cellular elements, in their normal condition at least, the most complete coincidence with the lymph; it may, however, be remarked that it is not uncommon to meet in them with the large so-called granule spheres, which, when freshly examined, possess numerous contractile, constantly varying, extraordinarily fine fibrils or pseudopodia on their surface, and probably have swallowed the granules which are imbedded in their substance.

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CHAPTER X.

THE SPLEEN.

By WILHELM MÜLLER,

OF JENA.

THE structure of the spleen is intimately associated with that of the lymphatic glands. In both organs numerous trabeculæ proceeding from the capsule divide and subdivide, containing in many animals muscular tissue, the contraction of which effects a shortening of certain vascular channels and the evacuation of the fluids contained in the parenchyma. In both organs the cytogenous or adenoid tissue is employed to invest at least a portion of the bloodvessels with sheaths containing numerous cells, the rounded appendices of which, rich in capillaries, constitute the follicles of the lymphatic glands and the so-called Malpighian corpuscles of the spleen. In both organs the wall of certain vessels undergoes a peculiar modification, characterised by the breaking up of the tissue into a plexus of embryonal cells, the interstices of which are permeated by the fluids contained in their respective vessels; in the one case by lymph, in the other by blood. It is a consequence of this agreement in structure that certain causes of disease produce similar pathological effects in both organs, as is seen in typhus, leucæmia, and certain forms of glandular sarcoma (Hodgkin's disease).

The spleen is not present in all Vertebrata. In the Leptocardia and Myxinoids, for instance, it has not as yet been demonstrated. In the remaining Vertebrata, which possess the organ, it is constantly included between the laminæ of the peritoneum. Its position, however, is various; according to whether it is developed in the meso-gastrium, the mesentery proper, or the peritoneal investment of the pancreas. The structure, again, presents varieties in the different classes of the

animal kingdom; in the Ophidia and in the Saurians, the constituent which in all other Vertebrata is chiefly developed, is here rudimentary, whilst that which in the latter is an accessory apparatus, agreeing with the cytogenous vascular sheaths of the lymphatic and lymphoid glands, attains in the former its greatest development. In consequence of this mode of development, the spleen of these animals forms the link connecting the lymphatic and lymphoid glands to the spleen of other vertebrates. These peculiarities of structure justify us in proceeding to describe the spleen of Ophidia and Saurians separately from the remaining vertebrates.

THE SPLEEN OF REPTILES.—In Ophidia the spleen appears to the naked eye as a granular mass, situated at the upper

Fig. 64.

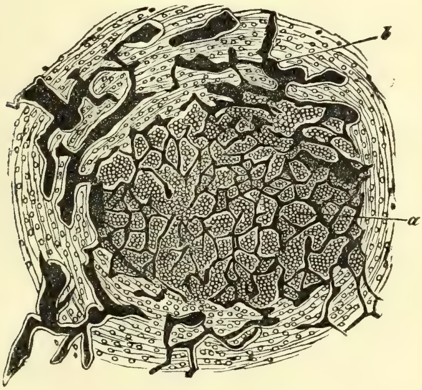

Fig. 64. From the spleen of the Tropidonotus natrix. *a*, follicle, with its capillary plexus; *b*, septum with venous plexus.

extremity of the pancreas; but in Mammals it lies on the left side of the stomach, and presents a more homogeneous structure. It possesses a capsule composed of fibrillar connective tissue and fine elastic fibres. The interstices of the fibrils of the connective tissue contain, especially in the middle layers of the capsule, numerous lymph corpuscle-like cells. The deeper layers exhibit, in preparations that have not been injected, regularly

arranged bands of smooth muscular tissue. In injected preparations a rich plexus of veins comes into view at this part, to the walls of which most, if not all, of the smooth muscles must be attributed.

The interior of the organ is traversed by septa given off at tolerably regular intervals from the internal surface of the capsule. The structure of these processes agrees with that of the capsule, and they intercommunicate with one another in the interior of the organ. They form stellate expansions; their connective tissue becoming infiltrated with lymph corpuscles, which in this modified form occupies all the interspaces of the proper parenchyma of the organ. This last appears in the form of spheroidal masses (globi or follicles), the diameter of which, in the ordinary domestic animals, varies from 0·5 to 0·75 millimeter. The follicles themselves are composed of cells and a retiform intermediate substance.

The cells agree with the lymph corpuscles of the animals in question, consisting of a mass of protoplasm containing a nucleus, but destitute of a cell wall. Larger morphological elements are constantly found intermingled with them, containing two or three nuclei which may be regarded as the result of a process of multiplication. At the periphery of each follicle the cells lie more closely packed together than near the centre, and in the fresh state they are connected together by a pale finely granular tenacious intermediate substance. In preparations that have been hardened by diluted solutions of chromic acid, a plexus of delicate fibres may be recognised. This plexus is more distinctly fibrillar, and its meshes are more elongated near the periphery of the follicle than elsewhere, and the interspaces are here also filled with closely compressed lymph corpuscle-like cells. This more compact plexus extends beyond the limits of the follicles, so that neither in the fresh nor in the hardened state can a continuous investing membrane be demonstrated around them.

The bloodvessels of the spleen of Reptiles consist of arteries, capillaries, and veins. The artery enters the spleen of Ophidians at the part opposite the pancreas, which is sometimes hollowed out in the form of a hilus, and runs towards the centre, enclosed in a membrane-like investment of connective

tissue containing numerous lymph corpuscles. At this part it divides into fine branches, which run towards the centre of the several follicles, where the smallest arterioles break up into a very characteristic capillary plexus. This forms meshes of 0·015—0·03 millimeter in width, which contain the parenchyma. The meshes are polygonal in form, strongly resembling the capillary plexuses of the fœtus; the calibre of the vessels exhibits, within a short space, variations of considerable extent, and the wall, whilst it in part corresponds precisely to that of ordinary capillaries, is in part constituted of distinct nucleated cells, which are with difficulty, and only through their somewhat more elongated form, distinguishable from those of the adjacent parenchyma. Near the periphery of the follicles the meshes of the capillary plexus diminish, whilst the diameter of the vessels increases in size, and they at length become continuous with a very close plexus of thin-walled veins, which wind around the follicles. These veins, which in some parts consist only of a thin connective-tissue layer containing numerous cells, transmit their blood into larger branches, lined with epithelium, and provided with layers of muscular tissue, which partly run along the septa in the interior of the organ, and partly in the deeper layers of the capsule, to reach the point of entrance of the artery, by the side of which they emerge from the organ as the splenic veins. The fact that the walls of a portion of the capillaries in the spleen of Ophidians very frequently present features reminding the observer of their embryonic structure, naturally suggests that besides a continuous new formation of lymph corpuscles, a similar neoplastic formation of capillaries may also take place, but what relation this process bears to the function of the organ is not at present known. The plexus of thin-walled veins which wind around the periphery of the follicles resemble the lymph spaces that surround the periphery of the follicles of the lymphatic glands. They represent at the same time the rudiment of a splenic pulp. If we imagine the elements of the walls of these canals to become developed into a plexiform tissue traversing the lumen of the vessel, we shall obtain a tissue presenting the essential characteristics of the splenic pulp, as it occurs in other vertebrate

animals. No observations have hitherto been made on the lymphatics or on the nerves of the spleen in Reptiles.

The Spleen of Fishes, Amphibia, Chelonians, Birds, and Mammals.—However various may be the structural arrangements of the spleen in these several divisions of the animal kingdom, the essential features of construction are the same in all. The organ is constantly invested by a capsule which sends off processes into the interior. These either hold some determinate relation to the venous system of the organ, forming venous sheaths, septa, and trabeculæ, or to the arterial system in the form of arterial sheaths. The interspaces of these tissues are filled with the peculiar parenchyma termed the splenic pulp.

The Capsule of the Spleen.—The thickness of the splenic capsule appears to bear a direct proportion to the whole volume of the organ. In the embryo it is invested by a short form of cylinder epithelium, resembling the ordinary epithelium of the peritoneum. As the organ grows this becomes flattened, and in adults forms delicate, partly square, partly rhomboidal plates. In all Vertebrata fibrillar connective tissue, with which elastic fibres are abundantly intermixed, enters into the composition of the capsule. In Fishes and Amphibia, so far as observation has at present extended, these elements form the entire capsule. In the higher Vertebrata, from the Chelonians upwards, a variable proportion of smooth muscular fibres, which are always situated in the deeper layers of the capsule, is likewise present. In Carnivora, in the Ruminants, and in the Pig, these are so largely developed, that the physiological experiment of merely dipping the spleen into warm water furnishes evidence of their presence, whilst in the Rodentia and Cheiroptera they are much less abundant. Muscular fibres, even if they are constantly present, are only sparingly distributed in the splenic capsule of Man.

Septa and Sheaths of the Veins.

The association of these two constituents is justified by the constancy of the relation which they bear to one another.

From the deeper layers of the splenic capsule fibrous bands are given off at regular distances, which are recognisable with the naked eye, and become continuous with cylindrical cords, the so-called trabeculæ of the spleen that penetrate its substance. They communicate with one another by lateral branches, and form a network traversing the entire organ. Their structure is identical with that of the deeper layers of the capsule, except that they for the most part contain bands of smooth muscular fibres. A certain number of these trabeculæ extend constantly between the ramifications of the veins, and become attached to their walls either at acute or at right angles. The structure of the latter is thus rendered more complex, as the splenic veins have already at their point of entrance into the organ received an annular investment from the capsule which soon coalesces with the vascular walls. The latter thus acquire remarkable firmness, and from the increased strength afforded by the attachment of the numerous trabeculæ are prevented from collapsing, presenting in consequence, in this respect, a certain similarity to the sinuses of the dura mater. This modified venous wall sooner or later becomes incomplete, whilst the connective tissue layers containing muscular fibres split into small bands, between which the lumen of the vessel is only limited by the epithelium layer and by a delicate layer of connective tissue containing numerous cells, and representing the tunica intima. This assumption of a fibrous character by the external vascular layers may even commence in the trunks of the splenic vein, as occurs in the Ruminants; but more frequently, as in Man, it is first observable in the smaller branches. The slender bands containing muscular fibres, into which the sinus-like venous wall divides, run for a greater or less distance along the branches, ultimately becoming detached and uniting with the trabecular network of the organ (W. Müller). The object fulfilled by the connection of the trabecular network of the spleen with the walls of the veins is sufficiently obvious. The longitudinal bundles of muscles belonging to the latter tend to shorten the canals, whilst the trabeculæ which are laterally attached to them widen them, and thus conditions favouring the discharge of fluid from them are established (Tomsa). A coincident contraction of the muscles of the capsule and of the

trabeculæ must, moreover, exert pressure upon the intervening parenchyma which compels the movement of such of the constituents of the latter as are capable of changing their position to those parts where the tension is least (W. Müller).

ARTERIAL SHEATHS.—At their entrance into the hilus of the organ the arteries receive a sheath from the capsule with which the proper vascular wall is loosely connected. This sheath consists of fibrillar connective tissue with numerous elastic fibres, and a moderate proportion of cell elements lying between the fasciculi, the latter appearing partly as rounded lymph corpuscle-like bodies, and partly as elliptical nuclei which only present small masses of protoplasm at their poles. The sheaths accompany the arterial branches, without essential modification in their structure, to the points at which the arteries and veins previously running together separate from one another, which usually occurs in the arterial branches, of from 0·3 to 0·2 millimeter in diameter. From this point onwards the arterial sheaths present a remarkable modification in their structure, which consists in the conversion of their connective tissue into a cytogenous tissue, whilst at the same time it becomes much looser in texture. The connective tissue bundles throughout the whole thickness of the sheath become coincidentally much looser; their fibrils become more delicate, and lymph corpuscle-like cells are abundantly found in their interstices. A cylindrical sheath, rich in cells, is thus formed, which accompanies the arterial branches either to their entrance into the blood passages of the pulp, as in Fishes, Amphibia and Chelonia, or to their passage into the capillaries, as in Birds and Mammals. In the first-named animals it is only seldom that any further development of these sheaths occurs; in Birds and Mammals, on the other hand, rounded or ellipsoidal sharply circumscribed bodies, varying from 0·3 to 1 millimeter in diameter, appear with great regularity, termed the Malpighian bodies of the spleen, which are easily recognisable with the naked eye, on account of their whitish colour. They represent, as is now generally admitted, local hyperplasiæ of the cytogenous connective tissue of the arterial sheaths. Their disposition upon the arterial branches to which they belong varies to some extent, according

to whether they are developed from the entire circumference of the arterial sheath, or from only a definite point of it; in the former case, surrounding the artery to which they belong like a ring; in the latter, being situated eccentrically, or being only laterally attached.

The parenchyma of the Malpighian bodies is formed of cells and a retiform intermediate substance; the cells agree in their characters with the lymph corpuscles of the several animals, and they are constantly found in various stages of development, some being smaller, with a single nucleus, and others larger, with several nuclei. Like those of the splenic pulp, they are capable of executing amœboid movements, and are usually more densely crowded at the periphery of the Malpighian bodies than at their centre. When treated with solution of carmine, *cæteris paribus*, they become more intensely tinted than those of the pulp, though it has not been hitherto determined whether the deeper hue is the consequence of the presence of a larger proportion of protoplasm capable of imbibing the colour, or to a difference in the fluid by which the protoplasm is permeated.

Associated with the cells is a delicate intermediate substance, the periplast of Huxley. This forms a network around the several cells or groups of cells, and when examined in the recent state, consists of a pale, extremely finely granular, tenacious material, which presents the form of delicate fibrils in preparations hardened in chromic acid. At the periphery of the Malpighian bodies the network becomes closer, the individual fibrils present a greater similarity to ordinary connective tissue fibrils, and the meshes become more elongated and narrow, though without actually forming a continuous membrane, as was first correctly demonstrated by Henle.

Pulp.—The tissue of the splenic pulp is composed of cells and of an intercellular substance. The former resemble the lymph corpuscles of the animal, and constantly appear as small uni-nucleated and larger multi-nucleated cells, furnishing evidence of the occurrence of continuous processes of new formation. These become less deeply tinted with carmine than those of the Malpighian bodies, which they, however, resemble in

exhibiting amœboid movements (Cohnheim). There may be frequently found in the splenic pulp, especially in adult animals, large cells which either contain granular pigment presenting the characters of Hæmatoidin, or rounded bodies resembling coloured blood corpuscles. We may presume that the greater number of these cells containing blood corpuscles are occasioned by the migration of coloured blood corpuscles into the protoplasm of the adjoining pulp cells.

The cells of the pulp are connected with one another by means of an intercellular substance. This was first observed by Tigri, and was more minutely described by Billroth. When examined in the fresh state, this appears as a pale, feebly refracting, very finely granular, tenacious substance, forming a delicate network between the protoplasm of the several cells. In chromic acid preparations it assumes the character of a tissue composed of homogeneous intercommunicating fibres.

At the periphery of the Malpighian corpuscles it becomes continuous, without any sharply defined line of demarcation,

Fig. 65.

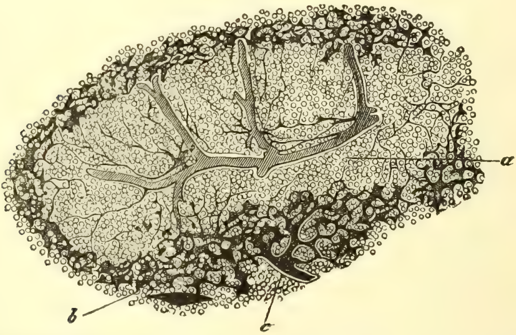

Fig. 65. From the spleen of the Hedgehog. *a*, a Malpighian corpuscle, with its vascular apparatus; *b*, splenic pulp, with the intermediary blood passages; *c*, the rootlets of the veins.

with the intercellular substance of the cortical layer. Near the capsule of the spleen, and also near the terminations of the capillaries and the origins of the veins, the intermediate substance becomes more strongly refractile as regards light, and more distinctly fibrillar. It here becomes continuous on the

one hand by numerous processes with the connective tissue of the capsule, and on the other hand with the tunica adventitia enveloping the capillaries and rootlets of the veins.

The cells and intercellular substance of the pulp are not so closely compressed as are those of the Malpighian bodies; on the contrary, they frequently leave rounded or lacuniform spaces between them, in which, in spleens recently removed from the animal after ligation of the vessels and exposure to the action of chromic acid at 0° Cent., coloured blood corpuscles constantly occur.

Bloodvessels of the Spleen.—Several arterial and venous trunks usually penetrate into the interior of the spleen at the hilus. Both sets of vessels, invested with their sheaths, run for some distance in proximity to each other, branching like a tree as they proceed. When they have diminished to a diameter varying from 0·3 to 0·2 millimeter, the arteries separate from the veins. Their mode of branching continues to be tree-like without the occurrence of anastomoses between the branches. In this course the arteries give branches to their investing sheaths which break up into a capillary network, presenting few and wide meshes. This capillary plexus is richer in the Malpighian corpuscles, the meshes being particularly small near the periphery. The calibre of these capillaries, as a rule, is moderately small, but frequently unequal, and the structure of the wall also exhibits varieties, sometimes presenting the characters of fully developed and sometimes of embryonic capillaries (Huxley, W. Müller). At the surface of the Malpighian corpuscles the capillaries either open into the intermediate blood passages or into the rootlets of the veins. No proper veins accompany the arterial sheaths from the point at which they become cytogenous.

The arteries, as is usual amongst the Mammalia, quickly divide into numerous capillaries, that run a long course, and are invested by a delicate tunica adventitia composed of connective tissue. Generally speaking they exhibit the structure of fully developed capillaries, but in some places they present for a considerable distance, walls composed of separate cells rich in protoplasm, constituting the transitional vessels of

Schweigger-Seidel. After a longer or shorter course the capillary wall becomes much attenuated and finely granular, the nuclei surrounded with a distinct mass of protoplasm, their continuity interrupted, and finally the homogeneous wall breaks up into small striæ, to which the cells are attached, and which are continuous with the cellular and fibrous plexus of the pulp. Through the spaces thus produced in the primary capillary wall the blood escapes into the cavities formed by the cellular and fibrous plexuses of the pulp, that is to say, into the intermediate blood passages. From the latter the blood is collected into the rootlets of the veins. These commence as cribriform, interrupted canals, the boundaries of which are essentially formed of lymph corpuscle-like cells and a delicate intercellular substance, constituting a plexus with numerous lacunæ. After a short or, as in man and rabbits, a somewhat longer course, the vein obtains a continuous internal investment, consisting of a layer of fusiform epithelial cells with spheroidal nuclei, which not unfrequently project into the lumen of the vessel, the superjacent connective tissue layer becoming at the same time condensed, causing the lymph corpuscle-like cells to crowd more closely together, and the fibrillar intercellular substance to become more distinct, whilst it pursues a transverse direction, and forms a tolerably close plexus (Henle). The smaller venous branches unite like the branches of trees to form larger trunks, investing which a tunica adventitia, consisting of longitudinal connective tissue fibrils with interspersed cellular elements, soon makes its appearance. The cylindrical muscular fasciculi belonging to the adjoining trabeculæ attach themselves longitudinally to these branches, and immediately become firmly adherent to their walls. As this occurs every now and then at different points, the gradually enlarging venous ramuscules obtain their already described compact walls, resembling those of the sinuses of the dura mater, and which they retain up to their point of exit from the organ.

The foregoing description of the arrangements of the circulating apparatus in the spleen rests (1) on the observation that, in recently hardened spleens still containing blood, both in the embryo (Peremeschko) and in the adult (W. Müller), the tissue of the pulp is con-

stantly traversed by blood corpuscles ; (2) upon the observation that artificial injections of the spleen constantly fill the same spaces which naturally contain blood corpuscles (W. Müller) ; (3) on the observation that, after the injection of the very fine seeds of the lycopodium, their presence in the pulp may be constantly demonstrated with the aid of the tests exhibiting the reactions of starch (Tigri). In opposition to this view is a second, which, originally advanced by Billroth, Grohe, Sasse, and Gray, has recently been supported by Kölliker. According to this view, the spleen, like other organs of the body, possesses a completely closed vascular system of ordinary structure, the veins everywhere forming plexiform anastomoses between which the parenchyma, traversed by capillaries, is contained in the form of cords, constituting the intervascular tissue cords of Billroth, or the bulbs of Grobe and Sasse. I have already, in my work on the spleen, explained why I cannot adopt this view. Moreover, in a series of the injected spleens of rabbits, and in the spleen of a monkey which was placed at my disposal by C. Thiersch, and more recently in examinations made upon the amyloid spleen of man, I have been unable to discover any facts favourable to the view maintained by Billroth and Sasse. Kölliker adduces in its favour, besides the points already mentioned, (1) that the current of blood would experience too much obstruction were it to freely traverse the pulp ; (2) that the fresh spleen constantly presents an acid reaction ; (3) that since the appearance of my work, no one has expressed himself in favour of the views therein contained ; (4) that this view would constitute a novelty. The first objection is opposed by comparison of the blood pressure in the arteria lienalis with the pressure of the lymph in the vas afferens of any group of lymphatic glands. The second is easily confuted by applying the best neutral litmus paper ; the third is overthrown by the work of Peremeschko, who is the only author that has thoroughly entered into the consideration of the question.

Lymphatics of the Spleen.—It is highly probable that the spleens of all vertebrate animals possess lymphatic vessels. They are divided into a superficial and a deep set. The former run in the capsule, and constitute a close plexus, from which trunks arise that pass with the trabeculæ into the interior of the organ, in order to anastomose there with the deeper set (Tomsa). The latter, as usual, accompany and form open networks between the arteries and their sheaths, and extend to near their terminations. According to the observations of

Tomsa, they penetrate the cytogenous sheaths of the vessels and their circumscribed enlargements, forming a plexus which, near the periphery of these structures, is only incompletely surrounded by the cavities of the adjoining pulp.

Nerves of the Spleen.—The nerves of the spleen also accompany the arteries in their course. They consist chiefly of Remak's fibres. They appear, in part at least, to terminate in peculiar organs that invest the capillary terminations of the vessels (W. Müller). These organs form ellipsoids, in the long axis of which a single capillary vessel runs. The substance of the ellipsoid consists of a pale, very finely granular substance in which oblong nuclei are imbedded (Schweigger-Seidel and W. Müller). These are highly developed in the spleens of Birds and carnivorous animals, but are only rudimentary in those of Rodents and of Man. In the interior of their granular mass fine fibres of Remak occur, the mode of termination of which has not as yet been actually determined. They require further investigation.

Development of the Spleen.—In all Vertebrata the spleen proceeds from a segment of the peritoneum. The situation of this segment differs in the several classes. In Ophidia it is the peritoneal investment of the upper extremity of the pancreas; in Fishes, Frogs, and Chelonia, it is the mesentery of the small or large intestine; in the Salamanders, Lizards, Birds, and Mammals, it is a prolongation of the mesogastrium from which the organ is developed. Its first appearance occurs in the form of a homogeneous thickening of the peritoneum, caused by increase of the embryonic formative cells of which it is composed. This thickening occurs very early in Man; it is already demonstrable at the period when the first budding out of the pancreas has made its appearance. At this time bloodvessels may be followed to the seat of the rudiment of the spleen (W. Müller).* At this period there may be observed in chromic acid preparations a very delicate pale network intervening between the embryonic

* Their relation to the first appearance of the spleen requires further investigation.

cells; but whether this proceeds from the outgrowth of a few cells, as Peremeschko maintains, or from the detachment of the peripheric protoplasm of numerous cells, I am not able to decide. The further development of the organ occurs tolerably rapidly, so that in the human fœtus of eight centimeters in length the various constituents are already differentiated. The cells lying beneath the peritoneal epithelium become elongated, and form fusiform nucleated bodies, and similar ones at an early period invest the larger vessels. From both small processes are given off, which grow towards one another, and represent the commencement of the trabecular system. Along the arterial branches, denser accumulations of small nucleated cells may already be discerned, which are conspicuous in tinted preparations by their deep colour, and these form by far the chief constituent of the pulp. This consists of cells with from one to three nuclei and a delicate intercellular substance, forming plexuses, the interstices of which are constantly filled with blood corpuscles. According to Peremeschko, there are now developed larger protoplasmic corpuscles in the tissue of the pulp containing from two to six nuclei, that are capable of performing amœboid movements, and which, towards the end of embryonic life, atrophy. In the further course of development the several constituents increase in volume, and a part of the fusiform cells of the capsule and the vascular sheaths develop into smooth muscular tissue. The arterial sheaths, containing numerous cells, are clearly distinguishable from the pulp, and from the middle of embryonic life the Malpighian corpuscles are recognisable. The cavities of the pulp may, about this time, be artificially injected (Peremeschko). From the commencement of differentiation of the several constituents of the organs, as this author has pointed out, the cells of the pulp appear paler and more delicate than those of the arterial sheaths. To explain this it must be borne in mind that both of these morphological elements develop from different textural formations, the pulp developing from the walls of the rootlets of the veins, the arterial sheaths with their Malpighian bodies from the connective tissue investing the arteries. It is of importance to establish this difference, because it furnishes the key to a series of comparative anatomical and pathological observa-

tions. Up to the present time, no facts have been ascertained in regard to the development of the lymph passages, or of the nerves of the spleen.

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CHAPTER XI.

THE THYMUS GLAND.

By E. KLEIN.

In Man and Mammals, at an early period of their existence, a placentiform lobulated body, called the thymus gland, which in point of structure must be associated with the peripheric lymphatic glands, lies behind the upper part of the sternum, and partly occupies the Incisura jugularis at the lower part of the neck. It is invested by a capsule rather loosely connected with the organ by means of vessels and fasciculi of connective tissue, the thickness of which increases with the size of the organ. The number and size of the lobes vary to a considerable extent. In dogs, in the pig, and in the cat, there are usually only two closely connected lobes of unequal size, which present an acute edge externally and below, but are remarkably thick at their surfaces of contact. In the calf, on the other hand, the organ consists of two oval placentiform lobes not presenting acute edges, and of nearly equal size, united together by a short cylindrical intermediate portion. The thymus of the new-born infant exhibits two or three lobes; when there are three, these are so arranged that a central thicker lobe has sometimes a larger and sometimes a smaller lobule on each side. The several lobules of the thymus in man, as well as in the dog, the cat, and the pig, may possess small appendices; and the fissures by which the lobes are produced are sometimes deep, and sometimes less strongly marked. Each lobe is divided into several lobules by fissures uniting at various angles, and these again are subdivisible into the ultimate divisions termed acini, alveoli, granules, or more correctly, follicles.

The capsule exhibits the usual structure of membranous connective tissue; its elements are, wavy connective tissue fibres

united into fasciculi of various sizes, which decussate in all directions, and thus form a tolerably resistant membrane; fine elastic fibrils, which are partly united in a plexiform manner, and partly form large arches running in an irregular manner between the fibres of the connective tissue; a few lustrous, broad, strongly refracting bands, characterised by their looped course and resistance to the action of acids; and, lastly, cellular elements. These either resemble colourless blood corpuscles, or are provided with processes like the so-called stellate cells, or they may appear as large, finely granular, irregularly shaped bodies, usually containing a single small, spheroidal, highly refracting nucleus. On the outer surface of the capsule, or that which is directed towards the thoracic cavity, a single layer of pavement epithelium, resembling in form and character that of the peritoneum, may easily be demonstrated. The cells of this layer are polyhedral, and slightly elongated or rhombic in form, containing a vesicular spheroidal or elliptical nucleus.

If a portion of the capsule, carefully detached from the recently removed thymus of a dog, be spread out upon the slide with the aid of some indifferent fluid, and examined with a high power, besides the tissues and structures above mentioned we may discern also the deeply situated delicate ramifications of the bloodvessels, together with the sparingly distributed trunks of medullated nerve fibres; and lastly, certain peculiar cavities. At the points where two or more strong fasciculi of connective tissue decussate we meet with such large usually elongated spaces, which have somewhat sinuous margins bounded by a single layer of fusiform disproportionately large cells; the tissue immediately external to these, and forming a kind of wall to the cavity, is but little condensed. It is clear that we have here to deal with the cavities belonging to the lymphatic system, respecting which it is difficult to state decisively whether they are simple lymph sacs, or are wide thin-walled lymphatic vessels. It is worthy of remark, that the quantity of lymph corpuscles they contain is extremely small, and bears no proportion to the size of the space.

The tissue bounding the several follicles of the thymus, and dipping into the interior of the organ from the surface of the several lobules, consists of a network of connective tissue,

which, as may be particularly well seen in the thymus of the dog, is usually composed of fine fibres, arranged in the form of delicate rhombic meshes. These are generally filled with more or less closely packed large cells; but near the free surface of the follicles, where they are not confluent with one another, the cells are smaller and more crowded, whilst the tissue becomes so condensed as to form a kind of capsule. The individual follicles are either entirely thus encapsuled and isolated, as frequently occurs in the calf, or several may be united at their centric portion, as in the dog and man. On the whole, their structural characters are comparable with those of the Peyer's patches of the small intestine.

The form of the several follicles is elongated, spheroidal, or polyhedral, and those situated near the surface are always larger than those more deeply seated; those of the dog and calf are usually elliptical in form.

The finer structure of the follicles displays the same morphological elements, with the same relative disposition, as the ordinary lymph follicles. According to His,* fine capillary bloodvessels, proceeding from the vessels running in the septa, penetrate the follicles at numerous points of their surface, and in consequence of these frequent anastomoses, form a very close-meshed plexus. Between the vessels, and attached to them, as well as to the connective tissue of the septa, an exceedingly compact, but very delicate, network is extended, chiefly formed by the anastomosing branches of multipolar cells, in the interstices of which are numerous lymph cells; in addition a narrow-meshed network may be distinguished, resembling the above, except in the absence of cells, and in the greater breadth of the trabeculæ, especially at their nodal points. These narrow-meshed networks are the prolongations of the interalveolar or interfollicular lymphatic vessels. Lastly, there occurs a third kind of trabecular structure in the form of strong elongated fibres, which are stretched between adjoining vessels, or between these

* *Beiträge zur Kenntniss der zum Lymphsysteme gehörigen Drüsen*, Siebold and Kölliker's *Zeitschrift für wissenschaftliche Zoologie*, Band x., p. 333.

and the septa of connective tissue. These are not much branched, and are attached by means of conical longitudinally striated bases to the vessels.

The contents of the follicles, that is to say, of the trabecular structures, consist of cells, which, according to their size, may be arranged in three categories. Of these the first, and by far the most numerous, are ordinary lymph corpuscles; the second are larger coarsely granular spheroidal bodies, composed of protoplasm, and containing one or several nuclei; and the third are Hassall's concentric corpuscles, of which Ecker * recognises two forms, one simple and the other compound. The former are spheroidal vesicles, varying from 0·0075 to 0·009 millimeter in diameter, containing in the interior of their concentrically striated sheath sometimes only a homogeneous mass with fatty lustre, but sometimes a nucleus and granular material. These last are as much as 0·027 millimeter in diameter, and are composed of several simple vesicles that are collectively invested and united together by a concentrically striated membrane. Both species of the concentric bodies occur, according to Ecker, at every stage of development; yet with increasing abundance as the gland gradually advances to complete maturity.

VESSELS.—In the calf and in man the larger branches running in the follicular septa divide into numerous branches that everywhere surround the follicles. † The arteries give off capillaries that penetrate into their interior, and after communicating by transverse branches, run in a radial direction, and terminate in circular vessels. As a rule the latter do not quite reach the centre of the follicles, but become continuous with veins which accompany the arteries.

The distribution of the vessels in the thymus of the dog presents some difference from that which has just been described. Here the larger trunks situated in the septa give off branches that penetrate into the interior of the follicles, and then break up at the outer part into a capillary network, by which they

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* *Blutgefässdrüsen* in R. Wagner's *Handwörterbuch*, Band i., p. 115.

† Ecker, *loc. cit.*, and His, *loc. cit.*

are completely filled.* The very wide spaces charged with lymph cells, which immediately invest the follicles, are in communication, by means of finer vessels, with the central parts of the follicles. M. His regards these spaces as lymphatics; but, according to my observations, it must still remain doubtful whether they are lymphatic vessels or sinuses investing the follicles.

According to the older views,† the follicles are hollow vesicles invested externally by a structureless membrane, and internally by a layer of connective tissue, their cavities all communicating with a common central canal.

Jendrassik ‡ has demonstrated that the elementary parts of the thymus gland are solid lymph follicles, in the central part of which a cavity is formed by softening. I find that these cavities only occur in the follicles of the thymus in man and the calf, and not always even there. The central part of the follicle, which, both in man and the calf, consists of a network of cells with interspersed lymph corpuscles, after prolonged hardening, easily becomes detached during manipulation.

In regard to the physiological atrophy of the thymus, it consists, according to His, of a gradual breaking-down and infiltration of the glandular tissue with fat, which extends gradually from the septa and the surface of the follicles towards their interior; but even in the earliest period, when there can be no question of atrophy, small isolated groups of fat cells may be found in the investing sheaths of the follicles.

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* Kölliker, *Gewebelehre*, p. 485.

† J. Simon, *A Physiological Essay on the Thymus Gland.* London, 1845. 4to. Gerlach, *Gewebelehre* Mainz, 8vo, Lieferung, 2 and 3. Ecker, *loc. cit.*

‡ *Anatomische Untersuchungen über den Bau der Thymusdrüse, Sitzungsberichte der k. Akad. zu Wien.*, 1856, Juli-heft.

CHAPTER XII.

THE THYROID GLAND.

By E. VERSON.

The term thyroid gland is applied to an organ composed of a *framework* of connective tissue condensed externally to a more or less thick investing membrane, and traversing the interior of the organ in the form of strong trabeculæ; and, secondly, of *gland vesicles*, sustained by the framework, which, as their name implies, constitute structures similar to the acini of a gland, but completely closed and vesicular.

The vesicles of the thyroid gland are composed of a thin transparent hyaline membrane, lined by epithelium, the cells of which are arranged in a single layer, and in fresh, uninjured specimens appear longer than broad, and are provided with a spheroidal nucleus, which may itself include one or several nucleoli. In this condition, however, the epithelium of the vesiculæ is only encountered in quite young animals when examined with the microscope immediately after having been taken from the living animal. In a very short time, even under the eye of the observer, the free surface of the cell wall may be seen to project irregularly, and spheroidal tenacious and hyaline drops, which after some time coalesce in the centre of the vesicle, gradually develop from the bodies of the epithelial cells. Usually, however, delicate lines of demarcation may be recognised between them, giving a facetted appearance to the clump of escaped and coalesced cell contents. Before these drops become intimately fused with each other in the centre they frequently indicate the path they are about to pursue by pseudopodial processes which partly adhere to the cell wall. These contents, at a more advanced age, and under pathological conditions, are converted into colloid, though

they originally represent only the product of a physiological process.

The several gland vesicles present great variation in size, and even in adults some may be found which are of much smaller diameter than the largest of those discoverable in the infant. It appears that in extra-uterine life the progressive increase of the several gland vesicles, if any, is usually very small. On the other hand, in a human embryo of the fifth or sixth month, I have found their diameter to be 0·0252—0·0336 millimeter, whilst their diameter in the newly born already amounts to 0·1—0·16 millimeter, and may in adults exceed 0·2 millimeter. The gland vesicles of the tortoise are particularly well adapted for investigation, since they measure from 0·14—0·27 millimeter. Mammals possess in general very small vesicles, which sometimes, by their further growth, so press upon one another that the space required for the capillaries is only obtained by an inflexion of their opposite walls. Such conditions I found to occur frequently in the dog, where the walls of the vesicles form projections internally, in which the epithelial cells are seated like the voussoirs of an arch.

It is deserving of notice that the larger vesicles occupy the centre of the several lobules, or, where these are not present, the centre of the entire gland, whilst at the periphery they appear much smaller and are compressed and flattened in form.

The epithelial cells, as already mentioned, are always somewhat higher than broad, and do not vary remarkably either with age or with the species of animal. Thus, for example, in an embryo of the fifth or the sixth month they were from 0·006—0·0095 millimeter long, and from 0·004—0·005 millimeter broad; in adults they attain the length of 0·01—0·16 millimeter; in the dog, from 0·008—0·0126 millimeter; in the calf, of about 0·0105; in the tortoise, from 0·0168 millimeter, etc.

The framework of the thyroid gland is a direct continuation of the external investing membrane, and, like this, consists of fasciculi of connective tissue, with numerous elastic fibres and connective tissue corpuscles, which for the most part appear fusiform or branched. The organ is partially traversed by

stronger bands which, on the one hand, are connected with the investing sheath, and on the other, isolate large groups of gland vesicles. In this way the thyroid gland of man is divided into primary and secondary segments, the line of division between which is recognisable by slight furrows. In other cases, however, these strong septa may fail, and the whole glandular organ represent a continuous mass.

The connective tissue lying between the several gland vesicles of the individual segments is very sparing in quantity, and sometimes even it is difficult to discover between the walls of contiguous vesicles a few fibres accompanying the capillaries. Near the investing membrane, and between the peripheral vesicles, it is more abundant. If the fresh vesicles of the tortoise be isolated by means of needles, we find them invested by a fine network of fibres, which frequently bear branched cells.

The Arteries are large branches of the thyroid artery, and penetrate into the interior of the gland, following the course of the fibrous septa, dividing the organ into segments or lobules. Their branches accompany the secondary septa, and these again break up into large capillaries having a diameter of 0·006—0·01 millimeter, that form a network around the several gland vesicles from which again the veins take their origin. These, externally to the fibrous sheath, are characterised by the width of their lumen and the proportionate thinness of their walls.

The lymphatics, according to Frey, commence with cæcal extremities between the gland vesicles, and unite to form meshes surrounding the lobules, finally emerging from the surface of the organ as vessels of considerable size. The *nerves* appear as thick trunks of dark-edged fibres which adhere firmly to the vessels.

In man the thyroid gland appears to be composed of a median and two lateral lobules united by means of connective tissue. Other mammals, as the dog, calf, horse, etc., possess a thyroid gland consisting of two separated lobules lying on either side of the trachea.

A single median lobe occurs in Amphibia and Birds, which descends into the thoracic cavity.

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CHAPTER XIII.

THE BLOOD.

By ALEXANDER ROLLETT.

THE red blood of vertebrate animals consists in part of a solution of various substances—the blood plasma—and in part of very small corpuscular structures of peculiar form.

The corpuscles are so abundant and so equally distributed through the fluid medium, that their interspaces are of microscopic dimensions, and fresh blood consequently presents to the naked eye the appearance of a homogeneous red fluid. The individual corpuscles do not all agree with one another in their characters, and hence several different kinds may be distinguished amongst them.

In the first place, we may distinguish between the coloured and the colourless forms, the number of the former predominating in healthy blood.

The coloured corpuscles are more uniform than the colourless, amongst which several subdivisions must be made.

THE BLOOD PLASMA.—The blood plasma, or Liguor Sanguinis, when examined in the fresh state and in microscopically thin layers, is destitute of colour. If a drop of blood be removed for a short time from the living body of an animal, fibrin separates from it in a solid form. But in reference to the coagulation of the blood,* we shall here only discuss the microscopic phenomena presented by the fibrinous clot. The fibrin, when in small quantities, separates itself in the form of delicate fibres decussating at various angles, though when in large only

* Compare Kühne, *Lehrbuch der Physiologischen Chemie.* Leipzig, 1866, pp. 162 to 174.

very gradually, as often occurs in the blood of cold-blooded animals; or if larger quantities of fibrin quickly separate, the whole drop of blood solidifies, without any alteration of the microscopic appearances being perceptible. In this case the change that has occurred only becomes evident on moving or breaking up the mass when it has undergone coagulation.

If, on the other hand, we leave a few drops of blood for a little while to themselves, which may be best effected by attaching them to the under side of a glass cover in a moist cell, we shall observe that the coagulum embracing the corpuscles retracts from the borders of the drop, and that a zone of clear serum is exuded, which gradually increases in breadth.

Here also striæ and bands of coagulated fibrin may be isolated by breaking up the coagulum and thorough elutriation with water.

The fibrinous coagulum appears doubly refractile under the polarising microscope.

We shall hereafter revert to the behaviour of the blood corpuscles in the fibrinous coagulum.

The Red Blood Corpuscles.—A knowledge of the general structure of these bodies cannot here be discussed, but will be taken for granted in the course of the following observations.

After the blood corpuscles had once been seen by Swammerdam in the Frog in 1658, by Malpighi in the Hedgehog in 1661, and by Leeuwenhoek in Man in 1673, numerous observations were accumulated respecting them, perhaps even to a greater extent than upon any other* morphological element of the animal body. Up to the present time, however, no structural arrangements have been discovered in them with the microscope that can enable us to furnish an explanation of all or even of the greater number of the phenomena they display.

Compared with other morphological elements of the tissues, the red blood corpuscles appear so peculiar, and are so readily and permanently alterable by the action of numerous and often not obvious external influences, and present so many remark-

* For the older literature, see Milne Edwards, *Leçons sur la Physiologie et l'Anatomie comparée*. Paris, 1857, T. i., p. 41.

able appearances, that statements based upon mere analogy can only be received with the most profound distrust.

The results that have been obtained by direct observation and inquiry will therefore here first be given, in order that we may not become confused with theories that have been inconsiderately advanced; the views of various histologists, founded on their own investigations, will, however, be subsequently noticed.

FORM AND COLOUR.—Throughout the whole series of vertebrate animals two typical forms are presented by the red blood corpuscles. They form thin disks, the contour of which is either circular or elliptical. The circular disks occur in Man and Mammals, with the exception of the Camel and Auchenia. The two last-named genera have, like all Birds, Amphibia, and most Fishes, elliptical blood corpuscles.

Amongst the Fishes only a few Cyclostomata (Petromyzon, Ammocœtes) are known to possess circular disks.

A small drop of human blood, brought as quickly as possible under the microscope in the form of a thin layer, exhibits densely crowded coloured corpuscles.

Their colour depends upon hæmoglobin.* The individual corpuscles, however, do not appear red like pure hæmoglobin, or its concentrated solutions, but of a yellowish or green tint, perhaps on account of its small thickness, just as the same colour may be obtained if thin layers of concentrated watery solutions, or thick layers of diluted solutions, of hæmoglobin are examined, and this whether it be oxyhæmoglobin or reduced hæmoglobin, or a definite mixture of both. The red colour of the blood is only exhibited under the microscope when large numbers of blood corpuscles are examined superimposed on one another.

Where a number of the corpuscles thus lie upon one another, as may occur by chance in every small drop of blood, there may also be seen, as F. Hoppe,† Preyer,‡ and Stricker §

* Compare Kühne, *Lehrbuch der Physolog. Chemie.* Leipzig, 1866, p. 196.

† Virchow's *Archiv*, Band xxiii., p. 446.

‡ Max Schultze's *Archiv*, Band ii., p. 92.

§ Pflüger's *Archiv*, 1868, p. 651.

have shown, the characteristic absorption bands of hæmoglobin, providing that a spectrum apparatus of appropriate construction is connected with the microscope. Stricker has also demonstrated in the microscopic spectrum the conversion of the oxyhæmoglobin bands into those of reduced hæmoglobin on alternate exposure to O and CO_2.

The circumstance of the red blood corpuscles being the carriers of the colouring matter of the blood, confers upon them their obviously great importance in the organism at large, on account of the part which the hæmoglobin plays in the exchange of the respiratory gases.

As regards the form of the blood corpuscles when examined microscopically in fresh blood, the greater number of the isolated corpuscles will be found to present perfectly circular contours, and to be of nearly equal size (fig. 66, *a*).

The description that must be given of this form may be best

Fig. 66.

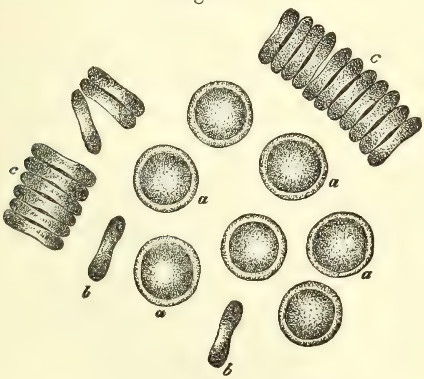


Fig. 66. Red blood corpuscles.

understood by making the corpuscles float by gentle taps on the covering glass. They then offer alternately the circular form and another completely different one, that, namely, of short rods with rounded poles and slightly hollowed surfaces, and resemble a finger biscuit, or a section carried through the axis of a bi-concave lens (fig. 66, *b*). Such a corpuscle, as it again revolves, places itself upon its edge again, and, in short,

gives the impression of a rotating disc, with a thinner central portion, caused by a fossa-like indentation of the surfaces and a thickened border. A solid model of the blood corpuscle may be represented by the revolution of the curve *c c c* (fig. 67) around the axis *a b*.

This form of blood corpuscle has also been termed the saucer-shaped. If the observer has convinced himself of the varying form of one and the same blood corpuscle, he will understand

Fig. 67.

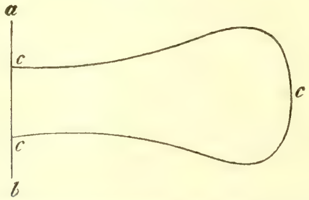


Fig. 67. Diagrammatic section of one half of a blood corpuscle.

how in every blood drop there are presented to his eye numbers of such corpuscles standing on their edge. Nevertheless, the number of those which are lying on their flat surfaces is always much greater.

Lateral views of the blood corpuscles are also very commonly obtained on account of the adherence of the corpuscles in groups to one another by their broad surfaces. Chain-like forms are thus produced, which, when viewed laterally, resemble rouleaux of coin (fig. 66, *c*). The cause of this formation of rouleaux, which is frequent in fresh blood, has not as yet been discovered. It does not occur within the vessels. It is seen not only in freshly drawn blood, but also in blood which has been immediately whipped, and thus freed from fibrin, though it may afterwards have remained for some time at rest.*

Besides the corpuscles just described, which are by far the most abundant, M. Schultze† constantly found in the blood of

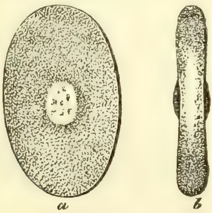
* See Rollett, *Wiener Akadem. Berichte*, Band i., Abth. ii., p. 183.
† *Archiv für Mikroskop. Anatomie*, Band i., p. 35.

himself and of a few other persons a small number, varying with the period of the day, of minute bodies, differing from the ordinary corpuscles in their spheroidal form and in some other peculiarities, together with transitional forms between them and the ordinary corpuscles. Further, in accordance with the frequently cited observation, though standing much in need of confirmation, of Lehmann,* the blood of the hepatic vein contains corpuscles of smaller size and more spheroidal form than usual, whilst those of the portal vein are of the ordinary kind.

The surface of the common form of corpuscle appears smooth, and the substance of the disk exhibits in its interior no indication of any difference in the index of refraction of its several parts. In passing from the centre to the circumference, however, there is a distinct change in the colour and transparency. In that position of the corpuscle in which the disk appears broadest and its edge most sharply defined, the centre is transparent, and the lateral portions are darker, whilst the extreme edge again presents a clearer ring. The latter is occasioned by the refraction which transmitted light experiences in the focal plane of the microscope when it traverses objects bounded by circular contours.†

The appearance presented by human blood corpuscles is dif-

Fig. 68.



ferent from that of the corpuscles of animals with elliptical corpuscles. External to the elliptical border of the flat surface of the disk there may be observed, at least in Birds, Amphibia,

* *Physiologische Chemie*, Band ii., pp. 85 and 232.

† Nägeli and Schwendener, *Das Mikroskop*, Theil i., p. 184, *et seq.* Harting, *Das Mikroskop*. Braunschweig, 1866, Band ii., p. 26, *et seq.*

and Fishes, a different structure when the disk stands on its edge. The optical section of the long axis appears here also slender, elongated, and rounded at the extremities. The long sides, however, have a projection at their centre (fig. 68, *b*). This prominence corresponds with an area situated near the centre of the disk, which, in comparison with the remaining coloured mass of the corpuscle, appears whiter than the rest. This is sometimes more or less circular as in the Bird, or elliptical as in the Frog, Triton, and land Salamander; it is often quite smooth, but also frequently presents fine indications of dark points or striæ.

This spot corresponds to a structure which possesses no analogue in the fully developed blood corpuscles of Man and Mammals, but behaves itself quite differently from the remaining substance of the corpuscle, and shows at least as great an amount of agreement with the structure termed the nucleus in other animal cells, as do the nuclei of the different cells with one another. In common with most histologists, we shall designate this structure as the nucleus of the blood corpuscles.

The fully developed elliptical corpuscles of the camel* and Auchenia are as destitute of a nucleus as the circular corpuscles of Man and other Mammals.

It thus appears that we may divide the blood corpuscles of animals into two classes, the nucleated and the non-nucleated. It must, however, be mentioned at once, that nucleated blood corpuscles occur at an early period of the development of the blood both in Man and Mammals.

SIZE OF THE RED BLOOD CORPUSCLES.—There is a large amount of literature bearing on the subject of the micrometric investigation of the blood.

The considerably differing results of the measurements that have been recorded have, for the most part, only a relative value. The micrometer employed has not, as a rule, been reduced to a definite standard. Exact comparison with a standard, it is well known, is no easy matter even for macro-

* Donné, *Cours de Microscopie*, etc., Paris, 1843, p. 70; *Comptes Rendus*, T. xiv., p. 367.

scopic measurement. But it is still more difficult in the case of the micrometer. Harting* and Welcker† have, on this account, detailed special methods by which the measurement of blood corpuscles may be accomplished.

As a rule, only the size of those blood corpuscles should be compared, which have been obtained by the same observer with the same instrument. It is self-evident also, when all the foregoing remarks are fully taken into consideration, that only those measurements are serviceable for comparison, in which an exact statement is made of the conditions under which they have been made.

Hence we must be on our guard respecting the inconsiderate employment of the various tables that have been published on the size of the blood corpuscles in different animals.‡ The absolute dimensions obtained by Welcker§ with a micrometer, are—

For man on an average expressed in millimeters:—

		Min	Max.
Diameter of disk . . .	0·00774	(0·00640	0·00860)
Greatest thickness of the disk	0·00190		

In six males and three females a minimum was observed of 0·0045 millimeter, and a maximum of 0·0097, all occurring between the terminal values, the smallest excepted, being very nearly of equal size.

The measurements were made on the corpuscles of fresh blood, or of blood dried in thin layers on glass.

The measurements given by Welcker for the small red corpuscles, described by Max Schultze, are 0·005—0·006 millimeter; and from these, gradual transitional forms may, according to Max Schultze, be traced up to those of ordinary diameter, from 0·008 to 0·010 millimeter.

We are indebted to Welcker for exact measurements of the

* *Das Mikroskop*, etc., Band ii., p. 288, *et seq.*

† *Zeitschrift für rationelle Medicin*, 3 R., Band xx., p. 259.

‡ The most extensive tables on this subject are to be found in Milne Edwards, *loc. cit.*, p. 84.

§ *Loc. cit.*, p. 263.

corpuscles in various animals, and a few of his mean values will be found in the subjoined note.*

The smallest corpuscles are those of the Moschus Javanicus. Amongst the largest are those possessed by the perennibranchiate Proteus anguinus, and the Siren lacertina (the long diameter of which amounts to $\frac{1}{16}$ mm. and the short to $\frac{1}{30}$ mm.).† The largest known, according to Riddel,‡ are those of the Amphiuma tridactylum, which are one-third larger than those of the Proteus.

Welcker§ employed a very short cylinder of plaster of Paris,

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* *Loc. cit.*, p. 279.

I. Circular Corpuscles.

Dog	0·0073
Cat	0·0065
Rabbit	0·0069
Sheep	0·0050
Goat (old)	0·0041
Goat (8th day)	0·0054
Moschus Javanicus	0·0025
Petromyzon mari.	0·0150
Ammocœt branch.	0·0117

II. Elliptical Corpuscles.

a, Long diameter; *b*, short diameter.

	a.	*b.*
Lama	0·0080	0·0040
Pigeon (old)	0·0147	0·0065
Pigeon (fledged)	0·0137	0·0078
Pigeon (fledged)	0·0126	0·0078
Duck	0·0129	0·0080
Fowl	0·0121	0·0072
Rana temporaria	0·0223	0·0157
Rana temp. (dry)	0·0214	0·0156
Triton Cristatus	0·0293	0·0195
Proteus (1 and 2)	0·0582 0·0579	0·0337 0·0356
Sturgeon	0·0134	0·0104
Cyprinus Alburn.	0·0131	0·0080
Lepidosiren Annectens	0·0410	0·0290

† Milne Edwards, *loc. cit.*, p. 89.

‡ *Journal de la Physiologie*, Band ii. Paris, 1859, p. 159.

§ *Loc. cit.*, pp. 265—275.

the proportion of the radius to the height of which was estimated to correspond with the dimensions of the blood corpuscles; and by scooping out the surface, and rounding off the edge, he obtained a curvature of the surface, which, to the eye (!) was similar to that of the blood corpuscles (compare fig. 67). He thus determined the mean volume of human blood corpuscles to be 0·000,000,072,217 of a cubic millimeter. Welcker, moreover, carefully lined the interior of this model, which was 5,000 times larger than the corpuscles, with paper of uniform thickness, then weighed the paper used, and compared this with the weight of a known superficial measure of the same paper. From the data thus obtained he estimated that the superficies presented by a blood corpuscle amounts to 0·0,001,280 square millimeter. It is sufficiently obvious that these numbers have only a coarsely approximative value.

Number of the Red Corpuscles.

Estimates of the number of the corpuscles have also been undertaken with the microscope. This method was suggested by Vierordt, and has been modified by Welcker.*

Their direct enumeration may be accomplished in the following way:—

A measured volume of blood is diffused as equably as possible in a thousand times its volume of an indifferent fluid (six grammes of Na. Cl. in one litre of water, according to Welcker), a small quantity of the mixture is taken up in a capillary tube of known calibre, and the length of the thread of fluid is estimated under the microscope by means of a micrometer. When the contents of the tubule have thus been ascertained, they are quickly distributed with a little solution of gum upon a slide, and the whole is allowed to dry. The preparation is covered with a micrometer divided into squares, and the corpuscles in the several squares can then be successively counted. In one experiment Vierordt used 0·0005—0·0008 cubic

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* Vierordt, *Archiv für Physiol. Heilkunde*, Band xi., pp. 26, 327, 854; xiii., p. 259; *Grundriss der Physiol.*, 3. Auflage, 1824, pp. 8, 9. Welcker, *Prager Vierteljahreschrift*, Band xliv., p. 60; *und Zeitschrift für rationelle Medicin*, 3 R., Band xx., p. 280.

millimeter of blood, in which about from 2,000 to 3,000 corpuscles were counted in the space of an hour.

Comparative enumerations, with test specimens of blood diluted to various extents, and measured in capillary tubes of various widths, gave a difference of two to three per cent. in the numbers, and seldom amounted to five per cent.

In a cubic millimeter of the healthy blood of a man, 5,000,000 red blood corpuscles were estimated to be present.

From this, and from the above-stated dimensions respecting the volume and surface of the corpuscles, there appear to be in a hundred volumes of blood thirty-six volumes of corpuscles and sixty-four volumes of plasma. The surface of the corpuscles in one cubic millimeter may be estimated to amount to 643 square millimeters.

Vierordt, Welcker, and Stölzing have also counted the blood corpuscles of various animals.

Alterations of the Red Blood Corpuscles.

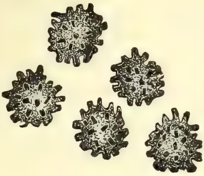
We shall now pursue another line of inquiry. Up to the present time, independently of the above-given enumerations, we have, as far as possible, considered the blood corpuscles in their normal condition. We are, however, indebted for much important information to the observation of certain changes which the corpuscles undergo under various circumstances, as well as to the results obtained from experimental histology.

For the purposes of inquiry into the nature of the red corpuscles, mechanical agents, the discharge of the Leyden flask, the application of induced and constant currents, exposure to heat and cold, and lastly, the addition of various chemical agents have been employed.

1. In freshly prepared specimens of human blood it may frequently be seen, after the lapse of a variable space of time, that the borders and surfaces of the corpuscles have lost their smooth aspect. The borders appear dentated; the surfaces, as may best be seen when the corpuscles are rolling over, are beset with little eminences. At the same time the corpuscles become smaller and more spherical (fig. 69). A few such corpuscles are often visible in fresh blood, immediately after it has

been drawn, so that it is difficult to determine whether they are pre-existent in it, whilst it is still circulating, or not. It is certain that, in blood abstracted from healthy persons, in many

Fig. 69.



instances, nearly all the corpuscles undergo this alteration, and this is stated (by Max Schultze)* to occur with still greater rapidity in those suffering from febrile diseases. The corpuscles thus altered have been described as mulberry-shaped, and the phenomenon regarded as a stellate contraction of the corpuscle. It was well known, long ago, to Hewson.†

The evaporation of water, and perhaps the cooling of the blood, are conditions favourable to these changes. But they may also occur, as will hereafter be shown, even when such conditions are not present. The appearances are presented by the corpuscles of Mammals, as well as by those of Man. And analogous phenomena are occasionally, though rarely, presented by the elliptical and nucleated corpuscles.

The blood corpuscles of Salamandra maculata, and of Triton cristatus and tæniatus easily assume a mulberry-like form under the microscope. In the blood of the Frog the phenomena first make their appearance as a consequence of the operation of external agents, and the corpuscles then become exactly similar to those of Mammals.

2. From the action of mechanical agents on the blood corpuscles we learn that their substance is composed of an extremely extensible and, within wide limits, completely elastic material.

That the blood corpuscles become elongated in their passage through the vessels, and that they also become curved in tra-

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* *Loc. cit.*

† *Opus posthumum*, pp. 19, 20.

versing the angles of division of the vessels, were facts well known to the older observers.

Lindwurm,* in thick solutions of mucilage; Hassall,† in microscopic coagula; and Henle,‡ in thick semi-fluid jelly, all saw the blood corpuscles assume a distorted or elongated and sometimes an extremely elongated fusiform shape.

The greatest variety of such forms is obtained when defibrinated blood is imbedded in pure solution of gelatine, melting at 35° to 36° C. (95° to 97° F.); from which, again, when it has become stiff, fine sections can be prepared, and placed under a covering glass; we may here particularly observe in such sections through the clefts of the gelatine, how the parts of the corpuscles drawn out into various forms, and often much attenuated, are always pale, and often even without perceptible colour; whilst the swollen parts appear, on the other hand, more deeply tinted. Long processes extend from some of the corpuscles, which ultimately divide without coalescing with others. The nuclei of the elliptical blood corpuscles are somewhat less yielding, and they are frequently found to be completely detached from the substance of the blood corpuscles; these, however, in many instances, as is deserving of special mention, do not in consequence suffer any notable change, either in their diameter or in their capabilities of resistance.§ Instances of the mechanical influences inducing change in the form of the red corpuscles occur, as already pointed out, in the movement of the blood while circulating. E. H. Weber,‖ in 1830, adduced his own observations upon this point, and referred to the numerous ones made previously to the time of Leeuwenhoek.

The phenomena may be well seen in examining the circulation in the membrane of the foot, and in the tongue or mesentery of the frog.

According to Rollett, in the circulating blood of Mammals, as, for instance, of guinea-pigs, that have been narcotised with

* *Zeitschrift für rationelle Medicin*, Band vi., p. 266.

† *Microscopic Anatomy*, p. 31, *et seq.*, plate ii., fig. 6.

‡ Canstatt's *Jahresberichte*, 1850, Band i., p. 32.

§ Rollett, *Sitzungsberichte der Wiener Akademie*, 1862, Band xl., vol. i., pp. 65—71.

‖ *Handbuch der Anatomie*, Band i. Braunschweig, 1830, p. 159.

opium, the red corpuscles of the blood do not retain their ordinary average form in the mesenteric vessels, when driven forward with the stream; but become, during their flow, more or less irregular in outline.* If the current be retarded or altogether arrested, or if the blood corpuscles are compressed against each other or against the interior of the vascular wall, they assume the same appearance as that which we have above described as characteristic of the fresh blood corpuscles. Moreover in diapaidesis, as it has been described from direct observation by Stricker,† Prussak, ‡ and others, the phenomena we are now considering may be observed in the red corpuscles during their transit through the vascular wall.

Lastly, it is to be observed that the blood corpuscles, notwithstanding their great extensibility, may be broken up by mechanical means. § This may easily be accomplished if a drop of fresh blood be quickly expanded into a thin layer by the pressure of a glass cover, which after the lapse of a few seconds is raised, and again firmly pressed down; there may then be seen coloured spheroidal or discoidal fragments. In nucleated corpuscles, as in those of the frog and triton, isolated nuclei are often visible, which are usually round, frequently distorted, and always granular. The number of the coloured fragments is always small in comparison with these, proving that the substance of the blood corpuscles becomes to some extent finely distributed through, or actually dissolved in, the surrounding fluid, which in point of fact appears slightly tinted. In anticipation of observations hereafter to be mentioned, it must be specially remarked that in these researches no shrivelled colourless shreds were noticed representing remains of the broken-down corpuscles.

3. The characters presented by the blood corpuscles on drying also deserve mention. C. Schmidt || has observed that when a thin layer of blood corpuscles is dried upon glass,

* *Sitzungsberichte der Wiener Akademie*, Band l., p. 196.

† *Loc. cit.*, Band lii., p. 386.

‡ *Loc. cit.*, Band lvi., p. 13.

§ Hensen, *Zeitschrift für wissenschaftliche Zoologie*, Band xi., p. 260. Vintschgau, *Atti dell' Instituto Veneto. Extr. dal* vol. vii., ser. iii., pp. 3—6.

|| *Die Diagnostik verdächtiger Flecke.* Mitau and Leipzig, 1848, p. 3, *et seq.*

they remain extended, and do not undergo any remarkable change in the dimensions of their larger diameter. Welcker* and others have corroborated this statement. The clear spot of the non-nucleated corpuscles, to which alone the above statement is strictly applicable, comes, under these circumstances, very distinctly into view, but passes without sharp definition into the surrounding darker parts.

The nucleated corpuscles do not remain quite unaltered in the dimensions of their surfaces; the variation is, however, of small amount. Many retain their form and smoothness; others become curved or sinuous. The clear spot corresponding to the nucleus, and its delicate markings, come more distinctly into view. In some corpuscles the nucleus, after drying, always appears very sharply defined, and separated from the remaining substance of the blood corpuscles by a clear reddish refractile border investing it like a wall, and making it appear as if lying in a cavity. In blood dried in masses the blood corpuscles are found to present manifold changes of form and to become ultimately attached to one another, so that it is difficult to recognise them in fragments of dried crust.

4. In the coagula which originate in the lymph sacs of frogs or salamanders after bleeding, according to Rindfleisch † and Preyer, ‡ coloured or colourless processes are protruded from the substance of the corpuscles, which are at first smooth, but afterwards resemble a string of pearls. According to Preyer, these can be again withdrawn, or may become completely isolated, or may separate into a few spheroidal masses. Beale § saw similar changes occur in the red corpuscles on a slide, in consequence of evaporation (? coagulation) and warming.

5. In order to observe the effect of electrical discharges ‖ and of induction currents upon the blood corpuscles, the arrangement exhibited in pp. 21, 22, of this manual may be employed, except

* *Loc. cit.*, p. 261.

† *Experimental Studien über die Histologie des Blütes.* Leipzig, 1863, p. 8.

‡ Virchow's *Archiv*, Band xxx., p. 417.

§ *Quarterly Journal of Microscopical Science*, No. 13, 1864.

‖ Rollett, *Sitzungsberichte der Wiener Akademie*, Band xlvi., pp. 92—97; Band xlvii. pp. 356—390; Band l., pp. 178—202.

that it is better to provide the copper pole with clips than with hooks. In these the ends of the induction coil or the ends of a transversely divided discharging rod of a Leyden flask are received, so that the tin-foil electrodes make a complete arc of union with the blood found between them and the wires. In order to enter more minutely into the phenomena which can be observed under the microscope, it is necessary in the first instance to bear in mind the results of microscopic experiments.

If the blood of a mammal be introduced into the arc of discharge of a Leyden phial, and a series of shocks be passed through it, it becomes altered, losing its opacity, and assuming a transparent lake-like tint. Microscopic examination shows that the blood corpuscles become altered, ultimately presenting only extremely delicate, pale, and feebly refracting particles. If in a consecutive series of examinations the number of the discharges requisite to produce the most complete transparency possible be taken as a measure of comparison for the clarifying power of the discharging current, we arrive at the following conclusions:—

The action of each successive shock is superadded to those which precede it.

The transparency of each element of the conductor formed by the blood is dependent on the intensity (density) of the current acting upon the unit of its transverse section with which it proportionally increases; it is also dependent upon the amount of what may be termed the specific resistance of the blood corpuscles, which differs in different kinds of blood, and with the increase of which, though not in a hitherto clearly ascertained ratio, the clarifying influence diminishes.

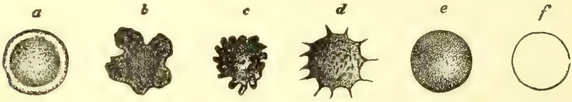
With a given specific resistance of the blood corpuscles, and with given size and specific conductivity of the blood, the course of the phenomena can be varied according to the quantity and mean intensity of the electricity in the phial.

The most advantageous distance of the tin-foil electrodes from one another for microscopic investigations is six millimeters; between these a thin layer of blood, covered with a thin plate of glass, should be introduced, and a Leyden flask employed, presenting a surface of about five hundred square centimeters, with a striking distance of one millimeter. Striking distances of greater extent cannot be used, as the

blood with the glass cover may be easily displaced, the sparks then passing directly from one electrode to another. Moreover, the surface of the flask must not materially exceed the above, or the discharging shock will occasion electrolysis (scarcely perceptible in the above-mentioned arrangement) to occur to an extent which may seriously interfere with the result. When these conditions are preserved, and the discharges are made to succeed each other at intervals of from three to five minutes, the following consecutive changes may be observed in the blood corpuscles :—

The circular disk-like corpuscles (fig. 70, *a*) in the first instance present one or two projections at their borders, and these gradually increase in number to three, five, or more.

Fig. 70.

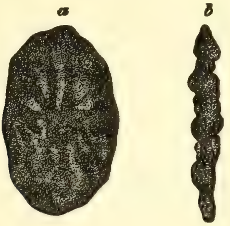


I have named this form the rosette form (fig. 70, *b*); it passes gradually into the mulberry form (fig. 70, *c*), which can always be produced at will by the discharge. To this succeeds a stage in which the processes become pointed, so that the corpuscles assume more the form of a paradise apple (horse chestnut) (fig. 70, *d*). Lastly, all the spikes are withdrawn, and a coloured corpuscle results (fig. 70, *e*),which then loses its colour, and a smooth colourless body is left (fig. 70, *f*), that long remains in the fluid in an unaltered condition.

In the case of the frog the blood corpuscles first assume a spotted appearance. Local thickenings then occur in the direction of the shortest diameter, which for the most part proceed radially from the nucleus (fig. 71, *a* and *b*). This, however, is not always the case; for it sometimes happens that the thickenings are nearly perpendicular to the longest diameter of the corpuscle, and cross it in the form of transverse bands. The latter is of most frequent occurrence in the blood of tritons. Upon this stage, which is obviously analogous to the first (fig 70, *b*) and to the second (fig. 70, *c*) stage in the blood corpuscles of

Mammals, there follows a stage in which the corpuscles again become smooth; their substance is then equably thickened, but the two other diameters have become somewhat smaller, whilst the mass either on one or both sides of the nucleus becomes swollen, so that the latter as it were closes a communication between the halves of a double funnel. At length the walls of

Fig. 71.



these funnels coalesce, and the corpuscles become egg-shaped or round. In the latter condition they are at first still coloured, but at a later period they gradually lose their colouring material, and there then only remains a dull colourless mass surrounding the nucleus. The nuclei appear somewhat rounded and more clearly visible in their interior.

Just as the coalescence of corpuscles may be observed to occur at the points where they are accidentally in contact, so it frequently happens that two or more blood corpuscles, when they have become coloured spheroids, completely coalesce with each other. The larger spheroids with numerous nuclei then lose their colouring matter just in the same manner as the individual corpuscles. Another highly remarkable phenomenon is that the nucleus may escape suddenly or gradually from the corpuscles. Non-nucleated coloured spheroids thus originate, which again gradually lose their colour. Neumann also has subjected the operation of induction currents upon the blood corpuscles to examination, and the phenomena he has observed agree in all essential particulars with those that have been above described.

On the other hand, the constant electric current does not produce these effects. It only produces alterations in the blood

corpuscles in the immediate neighbourhood of the metallic electrodes; those observed at the positive pole being similar to those effected by acids, and those of the opposite pole to those of the alkali which is there set free.* We shall hereafter enter more fully into the action exerted by acids and alkalies on the corpuscles.

6. After Klebs,† Rollett,‡ and Beale§ had originally described the influence of increased temperature on the red blood corpuscles, Max Schultze || first applied a more exact and methodic mode of investigation by means of the slide he has constructed, which is capable of being heated to a definite degree.

At about 52° C. (125° F.) the red corpuscles of man present first shallow and then deep fissures, which ultimately lead to the detachment of spherical masses. Some blood corpuscles assume various shapes, or thrust forth moniliform fibres. The latter forms immediately remind one of those found by Rindfleisch and Preyer in extravasated blood. Finally, spheroidal coloured drops are always found, so that the middle part of the original corpuscles corresponds to one of the larger of such fragments, which, varying in magnitude from this to an almost molecular fineness, are beset with smaller particles at their margin, or are surrounded by a series of them in a free state. The alterations described by Klebs as occurring at a temperature of 38°C. (100° F.) were not observed by Max Schultze. From observations made in a water bath, Rollett ascertained the temperature at which the blood corpuscles became spheroidal to be between 40° and 50° C. (104°—122° F.) The changes in the corpuscles, however, do not occur suddenly, but only after long exposure, and without the segmentation observed at 52° C. (125° F.)

Lake-coloured blood, according to Max Schultze, is first obtained when the temperature is raised to 60° C. (140° F.)

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* Rollett, *loc. cit.*, Band xlvii., p. 359; Band lii., p. 257. A. Schmidt, Virchow's *Archiv*, Band xxix., p. 29; *Hämatologische Studien*. Dorpat, 1865, p. 116. Neumann, Reichert and Du Bois' *Archiv*, 1865, pp. 682—690.

† *Centralblatt für die medicin. Wissenschaften*, 1863, p. 851.

‡ *Loc. cit.*, Band l., p. 192.

§ *Loc. cit.*

|| *Loc. cit.*, p. 1.

At about 53° to 54° C. (127° to 129° F.), Max Schultze observed the same changes in the blood corpuscles of the fowl as those that have been already described.

The corpuscles of the blood of the frog at about 45° C. (130° F.) become partially maculated and to some extent tuberculated on their surface, others assume the form of a finger-biscuit or of a dumb-bell, whilst a few become oval or spherical.

7. If blood, contained in a platinum vessel, be alternately frozen and thawed several times in succession, it likewise assumes a carmine colour.

The non-nucleated blood disks are deprived of colour without becoming materially diminished in size, or they will be found to have become spherical, or of smaller diameter, or only their feebly refracting colourless remains can be discovered.

In the corpuscles of the blood of the frog the nucleus is seen to be surrounded by a pale elliptical or circular area, or the colour of the blood corpuscle appears to be to some extent retained. Various forms are also found which appear indented or chipped off; finally here also the blood corpuscles lose their colour.

The extensibility and elasticity of the uncoloured remains of the blood corpuscles are similar to those of the intact blood corpuscles.*

In frozen blood the nuclei either still resemble unaltered nuclei, only somewhat more sharply defined, or they are spheroidal, enlarged, and appear as if composed of a delicate framework of highly refractile substance, in the meshes of which a less strongly refractile substance is contained. These spaces are often but few in number. Frequently only a single space is present, in the form of a large vacuole surrounded by a ring of refractile material. These characters of the nucleus deserve attention in regard to facts that will hereafter have to be mentioned.

8. In reference to the phenomena that are occasioned by the addition of fluids to the blood corpuscles, three different conditions under which they may occur must be clearly distinguished. The reagent may be intimately commingled with the

* Rollett, *loc. cit.*, Band xlvi., pp. 74, 75.

blood by mechanical means, in which case it is only possible to observe the final changes effected in the corpuscles by the reagent under the microscope; or the plasma or serum of the blood corpuscle may be washed away with the reagent, under the microscope, in the manner described at p. xx. of the introduction to this work, in which case, in order to prevent the corpuscles from floating off, it will be found advantageous to spread upon the slide a thin layer of a felt-like mass of fine clean asbestos, or of scraped Swedish filtering paper, and to place the blood drop on this; or, lastly, the blood and the reagent may be placed in close proximity with each other, and allowed to diffuse slowly.

It is only when, in the process of washing by the first method, the several blood corpuscles exhibit differences in their behaviour with the reagent that we are justified in concluding that an internal and original difference exists between them.

It is not permissible to draw this conclusion when the second and third methods are employed, or at least only providing that very great caution has been exercised; for if the uniformity of the mixture has not been constantly maintained, some of the corpuscles will necessarily be first and more energetically acted on by the reagent, and the amount of change in any instance will be proportionate to the duration of the exposure to its influence. We may very easily satisfy ourselves that the changes effected by one and the same reagent are very different during the first period of its action, and lead to other results than at later periods.

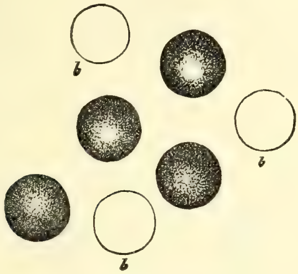
The many difficulties that encompass the study of the operation of reagents on the blood have not, as a rule, received sufficient attention; and less, perhaps, has been accomplished by this mode of experiment than might otherwise have been the case.

a. The addition of water renders the surface of the corpuscles smooth, and so changes their various diameters that they become spherical,* and thus acquire that form which with a given surface can contain the largest amount of material. This effect is commonly indicated as a process of imbibition, a

* Hewson, *Opus posthumum*, p. 25.

swelling up, although the diameter of the spheroid may be actually smaller than the long diameter of the corresponding disk (fig. 72). The spheroids are at first strongly coloured. On the cautious addition of water it may be frequently observed that the alteration of the primary form of the blood corpuscle to a spheroid does not occur with perfect uniformity in all the several and corresponding diameters, so that variable and

Fig. 72.



transitory unsymmetrical intervening forms are met with. In the nucleated ellipsoids it frequently happens that the nucleus changes its position in the corpuscle with a jerk,* whilst the corpuscle itself, as though in consequence of a recoil, is projected in the opposite direction. The nucleus then lies eccentrically in the corpuscle.

When water has continued its action on the corpuscles for a longer period, the spheroids become discoloured, and frequently produce the impression that their colouring matter is being gradually extracted; frequently also the colour disappears very rapidly, just as a hue of colour vanishes from a white surface when a coloured source of light by which it was previously illuminated is suddenly removed. The impressions thus given are precisely similar to those decolorations which have been formerly mentioned as the result of electrical discharges.

Smooth colourless bodies with feebly defined but smooth contour lines then remain (fig. 72, *b b b*).

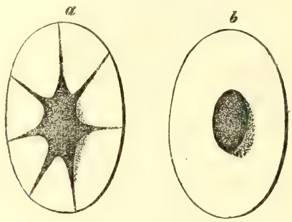
The nucleus which at the commencement of the action of

* See also the statements respecting the movements of the nucleus by C. H. Schultz. Preyer, *loc. cit.*, p. 437.

water, when the corpuscles have acquired a spherical form, comes more prominently into view, and remains so as long as these still retain their colour, but subsequently becomes less conspicuous, and after the long operation of large excess of water appears smooth, distended, and less highly refractile.

Especial attention should be directed to a structure which can be easily demonstrated in the elliptical corpuscles after the cautious addition of water (fig. 73). The still ellipsoidal corpuscle is bounded by a perfectly smooth contour line, but the place of the nucleus sometimes cappears to be occupied by a

Fig. 73.



coloured spheroid; whilst in other cases numerous processes radiate from this ball towards the contour line, becoming pointed peripherically. The parts lying between the latter and the coloured portion are homogeneous and colourless.

According to Kneuttinger,* these forms are obtained when fresh frog's blood, from which the fibrin has not been removed is mingled with three or four times its volume of water, and an examination shortly afterwards made of the gelatinous mass.

If larger quantities of water be added and thoroughly commingled with the blood, some of the corpuscles remain much longer in the condition of coloured spheroids than others; and the inference has been not unreasonably drawn, that an essential difference exists amongst such corpuscles.

b. Salts act very differently, according to their chemical nature and their degree of concentration. Many metallic salts occasion precipitates in the blood corpuscles similar to the acids

* *Zur Histologie des Blutes.* Würzburg, 1865, p. 21.

hereafter to be mentioned. The action of those salts which produce no precipitate (common salt, Glauber's salt, sal ammoniac, borax, magnesium chloride, and others) has been repeatedly described, in contrast to the action of water, as a shrivelling or contraction. Solutions of this nature cause the blood corpuscles to become less glutinous and extensible, their outline more distinct, their form curved, their surface wrinkled, and their border dentated. Such are the effects of moderately strong solutions of these salts. Very strong solutions of some of these salts, or the addition of the salts themselves, in powder, to the blood (common salt, Glauber's salt, magnesium chloride), only cause the blood corpuscles to shrink in the first instance, but soon they become round and pale, so that only colourless bodies remain.* In dilute solutions of some of these salts, the concentration of which is about equal to that of the blood serum, the corpuscles retain their characters for some time without alteration. Solutions of this kind are therefore frequently applied instead of serum for the purposes of dilution. With still greater degrees of dilution effects are produced similar to those that are observed when water is added in quantity to the blood.

A successive series of forms may frequently be observed to occur in the nucleated elliptical blood disks, on the addition of saline solutions of medium degrees of concentration, though they cannot be certainly caused to appear.

Hühnefeldt and Hensen† have obtained and represented forms similar to those above mentioned, by the agency of ammonia and sal ammoniac. They may also be observed on the applications of other saline solutions. They are almost identical with those that have been already described as resulting from the action of water (fig. 73). The blood corpuscles, however, appear equably maculated, coloured and colourless areas alternating with regularity; or, as frequently occurs in

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* Kölliker, *Zeitschrift für wissenschaftliche Zoologie*, Band vii., p. 184. Botkin, Virchow's *Archiv*, Band xv., p. 176. Bursy, *Ueber den Einfluss einiger Salze auf die Krystallisation des Blutes*, "On the Influence of some Salts on the Crystallization of the Blood." *Inaug. Diss.* Dorpat, 1863.

† *Zeitschrift für wissenschaftliche Zoologie*, Band ix., p. 261.

the blood corpuscles of Tritons, on the addition of three or four per cent. solutions of common salt, projections may form on the flat surface at right angles to the long axis, with paler or colourless spaces intervening between them.

The alkaline salts of the biliary acids, and the bile itself, according to the older observations of Plattner (1844), which Kühne* has corroborated by more recent researches, dissolve the red corpuscles of most animals, with phenomena in those of man which are similar to the effects that, according to L. Hermann, result from the action of chloroform or ether on the corpuscles. This subject, however, will be more fully discussed hereafter.

c. The action of sugar under the microscope is similar to that of the above-named salts. Its solutions, in moderate degrees of concentration, harden the corpuscles by the withdrawal of water, and forms are produced analogous to those that are met with after the action of moderately strong alkaline solutions.

d. Alkalies,† as a general rule, when in a state of moderate concentration, exert a solvent action on all the constituents of the blood corpuscles, including the nuclei. The following may be particularly mentioned amongst the many forms that are met with :—

In the case of potash and soda lyes, and of solutions of lime, baryta, and strontian, containing 0·1 gramme, in 100 cubic centimeters of water, a remarkable difference occurs, as compared with the action of pure water; for the corpuscles first change into coloured spheroids, but soon disappear without leaving a trace. In the nucleated blood corpuscles, on the other hand, after they have become converted into coloured spheroids, the nucleus may still be indistinctly seen, and appears to be expanded in its interior, though the diameter of the coloured spheroid is not itself materially altered. The corpuscle soon gives the impression of undergoing flattening, and immediately the whole spheroid, with the nucleus, entirely disappears. As already stated, the impression of the flattening occurs only in the nucleated blood corpuscle, but is visible both in the

* Virchow's *Archiv*, Band xiv., p. 333.

† Kneuttinger, *loc. cit.*, p. 39.

elliptical corpuscles and in the nucleated round corpuscles of the embryoes of Mammals. If the action of the reagent penetrating into the blood be rendered less energetic, the flattening still often occurs; and when all the rest of the corpuscle has quietly dissolved, the nucleus remains behind, enormously enlarged, and usually of a somewhat angular form, though homogeneous in its substance. This phenomenon, however, may be more frequently observed after the application of the alkaline earths, than after that of the pure alkalies. In regard to lime water, it deserves especial mention that, in many instances, after the coloured spheroids have been produced, and the corpuscles are about to flatten, the previously enlarged nucleus contained in the interior of the spheroid contracts suddenly to a strongly refracting body. The corpuscle then becomes pale, and this centrally situated body remains surrounded by a clear colourless area. This peculiar appearance occurs usually only at the commencement of the action of lime water.

e. Acids* readily occasion precipitates in the blood corpuscles. The precipitate either appears distributed through a clear transparent substance, surrounded by the circular or elliptical contour line of the corpuscle, which frequently expands suddenly with a jerk (acetic acid);† and coincidently the nucleus, which has become more highly refractile, and frequently somewhat angular or inflated, and darkly granular, comes more distinctly into view (acetic acid, diluted tincture of iodine), whilst it appears distinct from the colourless substance of the blood corpuscles, in consequence of being strongly tinted with hæmatin; or the precipitate occurs in the thoroughly granular or cloudy corpuscle, which appears as if hardened and usually somewhat shortened in its long diameter. When the acids act in this manner, the nucleus frequently appears to be not very sharply defined, but frequently shrivelled and surrounded by an empty space, as though lying in a cavity of the substance of the blood corpuscles (chromic acid, hydrochloric acid, nitric acid, picric acid, tannic acid, and concentrated tincture of iodine). When the acids are much

* Kneuttinger, *loc. cit.*, p. 28.

† *Idem.*

diluted, the second of the above-mentioned modes of operation frequently passes into the first, because in very diluted acids the action of the acid is complicated with that of the water.

The former of the above-mentioned effects is best exhibited by means of acetic acid, in solutions containing twenty grammes of pure acetic acid in 100 cubic centimeters of water, and upwards. The beautiful staining of the nucleus, with the colouring matter of the blood which then occurs, was first mentioned by Henle,* and has been corroborated by Kneuttinger;† it is exhibited in the most beautiful and convincing manner if the blood of a frog or triton is allowed to float into acetic acid: the blood sinks in the acid, and the dregs of the vessel can then be examined.

The non-nucleated corpuscles of Man and Mammals are first rendered spherical by the action of acetic acid, and then lose their colour, in which condition they remain for a considerable period.

Brücke‡ has subjected to a special investigation the changes that are effected on corpuscles of the fresh blood of the Triton by the action of a two per cent. solution of boracic acid, and we shall now proceed to describe them. Soon after the addition of the solution the corpuscles seem to be converted into ellipsoids, as after the action of certain proportions of water, the nuclei being often eccentrically situated; they ultimately, to a greater or less extent, become spherical. Forms are also obtained similar to those that have already been mentioned as occurring after the addition of water or saline solutions (fig. 73). In other corpuscles the nucleus alone appears of a deep colour, the remaining substance of the corpuscle being pale or completely colourless, and separated by a smooth contour line from the surrounding fluid, as after the action of many other acids in certain degrees of dilution. Direct observation of the action of boracic acid under the microscope renders it evident that the latter form does not necessarily proceed from any of the foregoing. In the greater number of

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* *Allgemeine Anatomie*, p. 431.

† *Loc. cit.*, pp. 28, 29.

‡ *Sitzungsberichte der Wiener Akademie*, Band lvi., p. 79.

instances the nucleus gradually becomes coloured, without the colour being discharged from the border of the corpuscle, although the substance of the corpuscle becomes proportionately colourless. A similar coloration of the nucleus occurs also with a two per cent. solution of boracic acid, when applied to the corpuscles dried on a slide. If the corpuscles are so modified by freezing, by shocks of electricity, or by ether or chloroform (the changes effected by which will be subsequently considered) that they have yielded up their colouring matter completely to the serum, and they are then treated with a two per cent. solution of boracic acid, the nuclei still acquire their deep tint from the colouring matter contained in the surrounding fluid. Brücke also observed the corpuscles discharge their nuclei from the action of boracic acid.

f. If it be desired to ascertain what alterations are effected in the blood corpuscles by small variations in the degree of acidity or alkalinity of the reagent, it is requisite, as has been shown by W. Addison,* in order to avoid the action of the water of the solution, to give a certain degree of concentration to the fluid by the addition of a small proportion of sugar or of salt. In such investigations it will be found, as he has correctly stated, that on the addition of an acid fluid, as of a solution of cane sugar weakly acidified with hydrochloric acid, the blood corpuscles possess, in all instances, smooth contours, and exhibit an increased degree of refraction; whereas on the addition of an alkaline fluid, as of a solution of common salt rendered feebly alkaline with liquor potassæ, the blood corpuscles become granulated and rough.

Appearances essentially similar are produced with still greater clearness by passing weak currents of electricity through the blood. That the corpuscles quickly become tuberculated and spinous in the vicinity of the alkaline pole was observed by Neumann,† who also saw the formation of the fibres described by Addison.

The change of form corresponding to the action of weak

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* *Quarterly Journal of Microscopical Science*, 1861; Jan., *Transact.*, p. 20; April. *Journal*, p. 81.

† *Loc. cit.*, pp. 679—681.

alkalies can, according to Addison, be changed by acid solutions into the form they induce, and *vice versâ.*

g. Urea,* in the state of fine powder, or in solution in water, in the proportion of from twenty-five to thirty grammes or less in 100 cubic centimeters of water, powerfully affects the form of the corpuscles, though they are not all affected in the same way.

In the blood of Amphibia some of the corpuscles always assume a curved form, and then small drops and spherical fragments become detached from them. Others become spherical without undergoing any further alteration in shape; but both large and small spheroids ultimately become colourless. During the assumption of the spheroidal form some of the corpuscles discharge their nuclei. The latter become slightly enlarged in the Frog, but much augmented in volume in the Triton, and then assume the remarkable appearance of a trabecular framework with large meshes. The nuclei which do not escape undergo similar changes if once the spheroid become colourless, so that the pale clear remains of the substance of the blood corpuscles appear as a kind of appendage to the enlarged nucleus. To regard these structures as nucleated albuminous spheroids escaped from adjoining coloured corpuscles is due to a misconception of the phenomena observed.†

If we now consider the action of less concentrated solutions of urea, we find that the incurvation of the corpuscles and detachment of drops is of rarer occurrence, and that the majority of corpuscles immediately become spherical, and at a subsequent period, together with the nucleus, entirely vanish. The incurvation of the border and the formation of drops is also exhibited by the non-nucleated blood corpuscles of Mammals when treated with urea.

h. Neutral solutions of carmine in pure ammonia (one gramme of carmine in 200 cubic centimeters of solution) produce on the

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* Hühnefeldt, *Chemismus in der thier. Natur.*, 1840, p. 60. Kölliker, *Zeitschrift für wissenschaftliche Zoologie*, Band vii., pp. 184, 253. Botkin, Virchow's *Archiv*, Band xx., p. 37. Hensen, *loc. cit.*, p. 264. Vintschgau, *loc. cit.*, p. 13. Preyer, *loc. cit.*, p. 432. Kneuttinger, *loc. cit.*, p. 56.

† Kneuttinger, *loc. cit.*, p. 58, fig. 9 *b*.

corpuscles the same effect as water. In the blood of Amphibia the inflated nuclei become, after a short time, tinged of a red colour. The blood corpuscles behave differently in the above-mentioned solutions of carmine in ammonia if from one-half to one per cent. of common salt be added, since they then remain apparently unaltered, and take up none of the carmine into their interior. On the other hand, the nucleus immediately becomes stained. If a mixture of blood and this coloured saline solution be allowed to freeze or be acted on by discharges of electricity, a series of remarkable phenomena may then be observed, upon the investigation of which I am now engaged.

If the blood of frogs or newts be allowed to flow into such saline solutions of carmine, there may always be found, besides the ordinary red and white blood corpuscles with nuclei, which long remain unstained, a few isolated free nuclei of an intense red colour. It thus appears that when unaltered the blood corpuscles do not absorb any colouring matter.

Rindfleisch* has described a remarkable alteration effected in the blood corpuscles of the frog by the addition of soluble anilin blue. They are then found to become nucleated spheroids, which quickly assume a blue colour, but it is only in solutions containing about a half-gramme to 100 cubic centimeters that the remarkable phenomenon of the discharge of the nucleus from the now spherical corpuscles occurs. It is especially remarkable that any part of the nucleus which once projects beyond the contour line of the corpuscle immediately swells up to a considerable extent, so that at this period the form of the nucleus resembles a short nail with a large head, which seems to have been driven into the substance of the corpuscle. When the nucleus has become altogether detached from the corpuscle, it swells up uniformly, becomes stained, and undergoes further changes, to be hereafter investigated.

i. Gases and vapours have lately, since the employment of gas cells, been likewise applied directly to preparations of blood under the microscope.

a. Stricker† has been especially engaged in investigating the

* *Loc. cit.*, pp. 10, 11.

† Pflüger's *Archiv*, 1868, p. 590.

action produced by the exposure of the blood corpuscles of the newt and frog alternately to carbonic acid and air.

So long as the blood remained unchanged he observed only the already-mentioned phenomena in the micro-spectrum, and was thus enabled to correct the older inexact statements.* Blood corpuscles changed by the action of water, however behaved themselves differently.

Stricker applied water in the form of vapour, by which means very fine gradations in the amount supplied can be attained.

On transmitting carbonic acid he then observed the occurrence of precipitates both in the nucleus and in the substance of the corpuscle; these precipitates vanished with oxygen, and returned with carbonic acid, and so on. Stricker considers these appearances, as had already been held by A. Schmidt and Schweigger-Seidel in the case of the precipitate obtained by the action of carbonic acid in the substance of the blood corpuscles of the frog, to be caused by the separation of paraglobulin; in order, however, to obtain such precipitates the addition of water must be carried almost to the extent of rendering the blood corpuscles colourless.

If smaller quantities of water be added, these precipitates do not occur. Under certain conditions the remarkable form appears that we have already described (fig. 73, *a*). This form, as an easily repeated experiment of Stricker shows, vanishes with an excess of carbonic acid. The blood corpuscles then appear once more equably tinted, and on the admission of air revert again to their original form.

With the addition of a certain amount of water the nucleus alone becomes tuberculated, and more sharply defined when carbonic acid is transmitted, whilst upon the passage of air it again becomes smooth. If this stage be exactly attained, the whole blood corpuscle may be seen to become spherical with carbonic acid, and again to assume its smooth form on the admission of air. Moreover, the thorn-apple form of the mammalian blood corpuscles can be made to disappear by car-

‡ Harless, *Monographie über den Einfluss der Gase auf die Form.* Erlangen, 1846. "Monograph on the influence of gases on form."

bonic acid, but can again be produced on the accession of air; the experiment, however, as Stricker has remarked, cannot be very frequently repeated, as the thorn-apple form ultimately remains persistent. A. Schmidt* showed that ozone gave a carmine tint to the blood by destruction of the blood corpuscles.

b. Ether,† chloroform,‡ bisulphide of carbon,§ and alcohol,|| conducted in the form of vapour over the blood, also render it of a carmine colour. If the appearances exhibited by the blood corpuscles are closely observed, it may be seen that in the circular disks the border becomes thickened,¶ and in place of the central depression a navel-like fossa appears. The funnel so formed becomes narrower and closes, and the corpuscles now appear as a coloured spheroid. Chloride of methyl vapour acts in a similar manner.** The above-mentioned vapours, but not the last, finally render the corpuscles colourless.

When ether and chloroform vapours act on the blood of the Amphibia, they render the corpuscles, in the first instance, spotty, though the colour subsequently becomes equably diffused, whilst the blood corpuscles appear to be somewhat diminished in size. On the other hand, the thickness of the border is increased, so that the nucleus lies in a depression. A few only of the blood corpuscles become spherical. The majority, when in the condition of a disc with thickened borders, lose their colour, and the nuclei then become more sharply defined. The blood corpuscles of the Amphibia also behave themselves similarly when air impregnated with ether or chloroform vapour is persistently transmitted over the preparation, and the phe-

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* Virchow's *Archiv*, Band xxix., p. 14.

† V. Wittich, *Journal für praktische Chemie*, Band lxi., p. 11; and *Königsberger Medic. Jahrbücher*, Band iii., p. 332. L. Hermann, Reichert and Du Bois' *Archiv*, 1866, p. 27.

‡ Chaumont, *Monthly Journal of Medicine*. Edinburgh, 1851, p. 470. Böttcher, Virchow's *Archiv*, Band xxxii., p. 126; Band xxxvi., p. 342. Kneuttinger, *loc. cit.*, p. 48. A. Schmidt and Schweigger-Seidel, *Berichte der König. Sächs. Gesellschaft der Wissenschaften*, 1867, p. 190.

§ Hermann, *loc. cit.*

|| Hermann, *loc. cit.* Kneuttinger, *loc, cit.*, p. 44.

¶ Hermann, *loc. cit.*, p. 31. A. Schmidt and Schweigger-Seidel, *loc. cit.*, p. 196.

** Hermann, *loc. cit.*

nomena do not essentially vary if the air thus charged with vapour is exchanged at definite periods for pure air.

If these reagents be added to the blood in a fluid condition, it will be found that ether and chloroform effect similar changes, except that a large number of blood corpuscles become spheroidal. Alcohol readily produces precipitates and irregular shrivelling.

OPINIONS RESPECTING THE STRUCTURE OF THE RED BLOOD CORPUSCLES.—In the exposition of these we need only go back to the time when the view which, though it had been advanced indeed before Schwann, yet was generally adopted only in consequence of his doctrine of the structure of animal cells, namely, that the red corpuscles are vesicles consisting of a membrane with fluid contents, began to be doubted.

The opponents of this view, after Max Schultze had, in 1861, demonstrated that a cell membrane is not a constant constituent of a cell, directed their attacks against the presence of a membrane in the red blood corpuscles. The presence or absence of a membrane must necessarily influence the conception of the nature of those constituents of the blood corpuscles which were formerly regarded as the coloured contents. In the criticism directed by Max Schultze against the cell theory of Schwann, the red blood corpuscles played a part, since in the discussion respecting the necessity of a nucleus to complete our idea of a cell, those of Man and Mammals were adduced as being destitute of a nucleus. This was for a considerable time almost universally taught, and of late has been opposed by Böttcher* alone. After what has already been stated in reference to the question of the nucleus, however, I do not consider it requisite to enter more fully into that subject, but shall refer to the communications of Böttcher, Klebs,† A. Schmidt, and Schweigger-Seidel.‡ We must deal differently with the question, whether the red blood corpuscles do, or do not, possess a membrane.

* Virchow's *Archiv*, Bände xxxvi. and xxxix.
† Virchow's *Archiv*, Band xxxviii.
‡ *Konig. Sächs. Gesellschaft*, etc., *Math. Phys. Classe*, 1867, p. 190.

It must, I think, in reference to this point, be admitted that important evidence, based on the form of the corpuscles, can be adduced against the view that they consist of vesicles in the sense held by a large number of histologists after the time of Schwann.

A vesicle filled with fluid, the parietes of which are yielding, and which again floats freely in another liquid, might be conceived to assume almost any form rather than of a body with two concave surfaces, as in Mammals, or with two convex surfaces, surrounded by a circular or elliptical zone of a certain thickness, as in Birds, Amphibia, and Fishes.

Schwann* adduced the assumption of a spheroidal form by the blood corpuscles on the addition of water, as a proof of their vesicular nature, maintaining that if they were not so they might indeed swell up and become colourless, but that they would retain their form like a sponge on the imbibition of fluid. The explanation of the action of water producing tension of the membrane, in consequence of the fluid contents of the vesicle increasing by endosmose, was at this time very generally accepted, just as the shrivelling of the surface, on the addition of saline solutions, was regarded as a consequence of a diffusion current setting from the interior. Brücke,† however, showed that neither the phenomena presented by the imbibition of water, nor after the addition of saline solutions, furnished conclusive evidence of the vesicular nature of the corpuscles.

If we base our opinion on the experiments performed on the red blood corpuscles by means of mechanical agents, we may exhaust all the various methods, without once meeting with a form which can be indisputably regarded as the torn and empty investing membrane, and the occurrence of which is in no other way capable of being explained; so again, whatever may be the changes that induction currents and electrical discharges, as well as freezing, induce in the corpuscles, no condition can at any time be seen directly proving the presence of a membrane.

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* *Ueber die Uebereinstimmung in Structur und Wachsthum der thierischen und Pflanzlichen Organismen.* Berlin, 1839, p. 74.

† *Berichte der Wiener Akademie,* Band xliv., p. 389.

On the contrary, the escape of the nucleus, the coalescence of the coloured spheroids, the physical character of the colourless remains after the discharge of the colouring matter, are all opposed to the existence of such an investment. The results of these inquiries are much more in favour of the view maintained by Rollett,* that a stroma or matrix enters into the structure of the coloured elastic extensible substance of the red blood corpuscles, which exhibits so remarkable a similarity in all animals, and that to this the form and the peculiar physical properties of the corpuscles are due. Hence the conclusion, that, however complicated the chemical constitution of the substance of the blood corpuscles may be, yet, by the action of a series of agents, the colouring matter can be separated from the stroma, without causing the latter to lose its essential characters.

The phenomena induced in the red blood corpuscles by various reagents, as urea, chloroform, and ether, and also the phenomena described by Max Schultze as resulting from the action of heat, fairly agree with this simple view. No doubt it may be urged that the membrane is highly extensible, and that it is reasonable to suppose that by the action of the above-mentioned agents it would be rapidly destroyed, rendering the phenomena observed consistent with its original presence around the tenacious semi-solid gelatinous contents of the blood corpuscles. But the theory that under these circumstances the membrane is really destroyed can only be based on the proof of its existence. We cannot hold the latter as ascertained if we regard the forms which a series of reagents (acids) occasion in the blood corpuscles; in the latter case we have much more ground for believing in the formation of artificial products, than they who hold the opposite view have reason in the previously adduced cases to admit the destruction of a naturally present membrane. The proof of the pre-existence of a membrane must here again, in the first instance, be furnished.

A circumstance bearing upon the question of a membrane is met with in the peculiar structures already frequently mentioned as occurring in the blood corpuscles of the Amphibia (fig. 73,

* *Loc. cit.*, Band xlvi., pp. 73, 94, 95, and 98.

a b). A retraction of the cell contents from the membrane has here been considered to occur, and we may associate with this the forms which Remak* and more recently Preyer† have described in regard to the fission of blood corpuscles, in which a gradually deepening furrow detaches a coloured portion of the blood corpuscle, whilst a glass-clear substance (the empty membrane) becomes apparent between the separating part and the investing contour line of the rest of the corpuscle.

Hensen,‡ who has devoted considerable attention to the first-mentioned forms, sought to explain the retraction of the contents from the membrane, the existence of which he believed, from his observations of these forms, to be proved, by ascribing a protoplasm to the red blood corpuscles, which invests the nucleus and lines the inner surface of the membrane (primordial utricle), these two portions being connected by delicate radially coursing fibres, in the spaces of which the closed cell fluid is ocontained; he supported this view especially upon the existenc of colourless fibres running in a radial direction from the nucleus, and it is well known that similar observations have been made by other histologists. But, independently of these fibres, which certainly do not represent any constant structure in the blood corpuscles, since they only appear to be met with under exceptionally favourable circumstances, the protoplasm distributed throughout the whole corpuscle must, according to the view of Hensen, form a considerable portion of their substance. The term protoplasm is now frequently so employed as to render it very desirable that its application should be restricted to a definite idea; but if we pay attention to the appearance and the most striking peculiarities of the protoplasmic masses described by Max Schultze§ and by Kühne;|| and if also, as will be subsequently discussed, we consider that in their development the red blood corpuscles are formed at the expense of the cells composed of contractile

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* Müller's *Archiv*, 1858, p. 178, Taf. viii.

† Virchow's *Archiv*, Band xxx., p. 417, Taf. xv., figs. 26 and 27.

‡ *Zeitschrift für wissenschaftliche Zoologie*, Band xi., p. 260, etc.

§ *Das Protoplasma der Rhizopoden uud der Pflanzenzellen.* Leipzig, 1863.

|| *Untersuchungen über das Protoplasma und die Contractilität.* Leipzig, 1864.

protoplasm, in which metamorphosis the essential characters of the latter, are lost, it is impossible to avoid expressing our opposition to the theory of Hensen. In fact, the forms which led Hensen to the above-mentioned view are susceptible of quite a different interpretation.

Brücke,* who observed such forms to be produced by the action of a two per cent. solution of boracic acid, considers that there is a porous structure composed of a non-contractile, very soft, colourless, perfectly transparent substance, which he further represents as the body of an animal, whose central part forms the nucleus of a nucleated corpuscle, and is free from hæmoglobin, whilst the remaining portion of the mass contains the whole of the hæmogoblin. Brücke considers that this latter portion accurately fills the intermediate spaces of the porous mass, and thus in combination with the parts free from pigment makes one continuous whole. To the colourless porous substance he has applied the term "*oekoid,*" whilst he calls the contained substance the "*zooid;*" and he is of opinion that the retraction of the zooid either completely or partially from the oekoidexplains the formation of the above-mentioned forms.

Stricker† agrees with Brücke in considering the oekoid to be the part enclosing the colouring matter, and as that which under certain conditions can retract towards the nucleus. He terms it the "body," at the same time attributing a greater amount of independence to the nucleus, and drawing attention to the analogy between the blood corpuscles of Amphibia and Mammals.

The question now arises, are the red blood corpuscles contractile as a whole, or is that part only contractile which is called the zooid by Brücke, or the body by Stricker?

Klebs‡ regarded the blood corpuscles of Mammals as contractile bodies, in consequence of his observations on the influence of temperature, though these have since been opposed by Max Schultze. The mulberry form he considered to correspond to the mobile condition, the curved-disk form to the quiescent

* *Wiener Berichte*, Band lvi., p. 79.

† Pflüger's *Archiv für Physiologie*, 1868, p. 591.

‡ *Centralblatt für die medicin. Wissenschaften*, 1863, p. 851.

condition, and the spherical form to the state of death. Rollett,* in consequence of his investigations upon the effects produced by electrical discharges on the blood corpuscles, is opposed to the view that they are contractile. He relies upon the facts that we always see the corpuscles in the interior of the vessels of the living animal in a state of merely passive movement; that blood corpuscles preserved outside the body for many months, or placed in blood destitute of oxygen but impregnated with carbonic acid, or in blood impregnated with carbonic oxide, behave themselves, when acted on by electrical shocks, in a manner essentially similar to those that have been recently taken from the living animal. Max Schultze† also, from his experiments on the influence of warmth on the non-nucleated corpuscles of Man and Mammals, arrived at the conclusion that these at least were not contractile; and Kühne‡ expresses himself in similar terms.

We arrive here, however, at a point at which it appears necessary to determine what signification must be applied to the term contractility. Brücke, in the treatise above alluded to, justifying himself in speaking of the contraction of the zooid as of a living being, remarks that it would profit us nothing were we to refer the separation of the zooid from the oikoid, not to a contraction of the former, but to a process resembling coagulation, and that we have no guarantee that we have arrived nearer to the truth. A movement which we may designate by the term contraction certainly occurs; for the coloured material unquestionably retreats from all sides towards the nucleus. What may be the causes of this contraction, and whether it may be compared in its essence with the contraction of a dying amœba, will probably long remain a subject of uncertainty; to the illumination of this darkness we may, however, soon attain.

Outline of the Chemistry of the Red Corpuscles.—The best-known constituent of the red blood corpuscles is hæ-

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† *Wiener Akad. Berichte*, Band l., pp. 190—200.

* *Archiv für Mikroskop. Anatomie*, Band i., pp. 33, 34.

‡ *Physiolog. Chemie.* Leipzig, 1866, p. 191.

moglobin; this can easily be obtained in the crystalline condition. Hæmoglobin crystals have long been known as blood crystals, and have been subjected to microscopical scrutiny.

In the first instance they were recognised accidentally, Reichert* having observed them in a preparation from the guinea-pig preserved in alcohol, in the form of tetrahedra. Fünke,† Kunde,‡ Schwann,§ at a later period obtained the crystals methodically from blood treated with water, and found that the crystals of colouring matter from the blood of different animals presented different crystalline forms, whilst those from the same animal were for the most part identical. Those from different animals were at first considered to belong to very different crystalline systems.

It has been more recently ascertained that blood crystals can not only be obtained by destroying the blood corpuscles with water, but that an entire series of conditions which render the blood carmine in colour by destruction of the corpuscles also lead to the production of hæmoglobin crystals. Thus, for instance, Rollett has shown that freezing and subsequent thawing of the blood, as well as the discharges of voltaic electricity; Rollett and A. Schmidt, that the alteration which the corpuscles undergo at the positive pole of a constant current; Max Schultze, that the elevation of the temperature of the blood by means of a water bath at 60° C. (140° Fahr.); Bursy, that the addition of powdered salt; V. Wittich, that the addition of ether, or transmission of ether vapour; Böttcher, that the action of chloroform; and Kühne, that the alkaline salts of the biliary acids, produce the same effect.

From each drop of such lake-coloured blood a large number of beautiful crystals may be obtained on the object slide of a microscope. Such crystals, obtained in constantly increasing numbers from different species of animals, and examined with still increasing care, are now proved to belong to two different

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* Müller's *Archiv, Jahrgang*, 1849, p. 197.

† *Zeitschrift für rationelle Medicin*, N. F., Band i., p. 172; Band ii., p. 199.

‡ *Idem*, Band ii., p. 271.

§ *Handbuch der Physiol. Chemie*, Band i., p. 365; Band ii., p. 151.

crystalline systems. Lang* was the first to show that what were regarded as regular tetrahedra from the blood of the guinea-pig, when examined with a Nicol's prism in a polarising microscope, appeared clear in four azimuths, and dark in four azimuths, and therefore that from their optical characters they belonged to the rhombic system: and further, that when compared with the prismatic crystals of human blood belonging to the same system, the following results were obtained. The lengths of the axes of the prisms of human blood present, according to measurements of the acute angle of the rhombic terminal plane (54° 1′), the proportion of 1 : 1,96 = 1 : 2·0,98; if then the second axis-length be divided by 2, the two axes would be of nearly equal length, which agrees well with the crystals from the blood of the guinea-pig.

The crystals of by far the greatest number of animals, however, occur either in the form of simple tetrahedra, or of tetrahedra with truncated angles and edges; or, like those of man, they form rhombic prisms, respecting which the recent treatise of Preyer† may be consulted. The blood crystals of squirrels alone, formerly described as six-sided plates, appear, as shown by Von Lang,‡ to be six-sided plates belonging to the hexagonal system.

Von Lang also first demonstrated that crystals of hæmoglobin, examined in two azimuths, with only one Nicol's prism over or under the object, exhibited colours different from those in the two intervening ones, and that they therefore present absorption phenomena in regard to light, in accordance with their crystalline form (Pleochroismus).

Besides hæmoglobin, a series of other substances have been ascribed to the blood corpuscles, constituting their colourless portion, which nevertheless appear to exist in very variable quantities in different animals. To these belong the albuminous bodies. The globulin, or paraglobulin of Kühne may be precipitated by means of carbonic acid from blood corpuscles mo-

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* *Sitzungsberichte der Wiener Akademie*, Band xlvi., p. 85, *et seq.*

† Pflüger's *Archiv, Jahrgang*, 1868, p. 365.

‡ *Loc. cit.*, p. 89.

dified to a certain degree by the action of water (Kühne, A. Schmidt, Stricker).

Moreover, an albuminous body, which still requires investigation, has been termed fibrinoid by Hoppe, and fibrin by Heynsius.

L. Hermann and Hoppe have demonstrated the presence of protagon, and Hoppe the presence of lecithin in the stroma of the blood corpuscles. As a consequence of the presence of hæmoglobin they contain a variable quantity of oxygen, and A. Schmidt has demonstrated the presence of carbonic acid in them. In addition to these substances there still occurs a certain proportion of salts differing qualitatively from the mineral matters of the plasma.

The Colourless Morphological Constituents of the Blood.—Amongst these the white corpuscles of the blood deserve to be first mentioned. These were distinguished by Hewson from the coloured, and the great majority are characterised by the lively movements they are capable of performing.*

Max Schultze,† who has lately carefully investigated these forms, distinguishes several kinds in human blood. First, round cells, not attaining the size of the red blood corpuscles, composed of a thin layer of cell substance, investing one or two nuclei, which last are either spheroidal or flattened by mutual compression.

With these may be associated other forms, equalling in size the ordinary red blood corpuscles, and, like the former, possessing nuclei. Lastly, finely and coarsely granular amœboid cells are met with, and various intermediate forms between them.

In freshly drawn blood these last appear as more or less rounded or irregularly shaped forms. At a temperature of from 35° to 40° C. (95° to 104° Fahr.) lively movements, resembling the creeping motions of an amœba, occur. When the temperature, however, is raised above 40° C., the movements cease, and the cells harden.

* Wharton Jones, *Philosophical Transactions*, 1846. Davaine, *Mémoire de la Societé de Biologie*, 1850, Tom. ii., p. 103. Lieberkühn, Müller's *Archiv*, 1854, p. 11, *et seq.*

† *Archiv für Mikroskop. Anatomie*, Band i., p. 9.

As long as they are in active movement they are capable of absorbing small particles of colouring matter, as of carmine and anilin blue, and also milk globules, into the interior of their bodies. In reference to the further peculiarities of these true protoplasmic masses, I must refer to the first chapter of this manual. Besides the white corpuscles of the blood, Max Schultze admits, as constant constituents of human blood, irregularly formed masses of colourless globules, which he regards as fragments of cell substance.

There is a statement frequently met with in books, that, under certain circumstances, fat drops are met with in the blood, often in such quantity that the serum acquires a milky appearance, as in sucking animals,* and after the use of oleaginous food.† Oily matters, which have entered the blood, seem however to disappear with great rapidity. In the remarks made upon Schlemm's observations on kittens, Joh. Müller‡ states that he only found milky serum when the animal had shortly before ingested milk.

Yet another morphological constituent occurs in the so-called elementary corpuscles of Zimmerman.§ These have been held to be generators of the blood corpuscles. The greater number of them, obtained in the mode adopted by Zimmerman, from blood treated with salt, can be easily recognised as artificial products; that is to say, as the colourless remains of distorted red corpuscles (Hensen). It is not a matter of surprise that similar forms should also be frequently found in freshly prepared blood (Kneuttinger). Lastly, Max Schultze has demonstrated that the smallest elementary corpuscles of Zimmerman agree with his before-mentioned granules.

As regards the number of the white blood corpuscles, they are much less abundant in normal blood than in the red, and their relative number is subject to much greater variation

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* Schlemm and Joh. Müller, Froriep's *Notizen*, Band xxv., 1829, p. 121.

† Kühne, *Physiolog. Chemie*, p. 181. Kölliker, *Gewebelehre*, 1867, p. 620.

‡ *Loc. cit.*

§ Rust's *Magazine*, Band lxvi., p. 171; Virchow's *Archiv*, Band xviii., p. 221; *Zeitschrift für wissenschaftliche Zoologie*, Band xi., p. 344. Hensen, *loc. cit.*, p. 259. Max Schultze, *loc. cit.*, p. 39. Kneuttinger, *loc. cit.*, p. 5.

The variations depend upon the age, sex, period after food, and the vascular territory from which the blood examined has been taken.

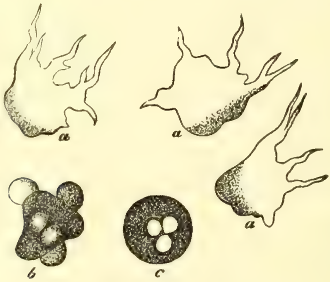
Under all these different circumstances the number of the white blood corpuscles has been counted, according to the methods adopted for the enumeration of the red.*

On the average there is, according to Welcker, one white corpuscle to 335 red, and according to Moleschott, one to 357.

Boys have one colourless to 226 coloured. Men, one to 346. Old men, one to 381. Girls, one to 389. Young women who are menstruating, one to 247. The same women, when not menstruating, one to 405. Pregnant women, one to 281 (Moleschott).

Hirt found in the early morning, and in the fasting condition, that the proportion was one white corpuscle to 716 red; half an hour after breakfast, 1 : 347; two to three hours later,

Fig. 74.



1 : 1,514; ten minutes after a midday dinner, 1 : 1,592; half an hour after the same, 1 : 429; two to three hours after the same, 1 : 1,481; half an hour after tea, 1 : 544; two to three hours after tea, 1 : 1,227.

In the splenic vein, Hirt found the proportion to be 1 : 60;

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* Welcker, Präger, *Virteljahrschrift, loc. cit.* Moleschott, *Wiener medicin. Wochenschrift*, 1854, No. 8. Hirt, *De Copia relativa Corpusculorum Sanguinis Alborum. Diss. inaug.* Lips., 1855. E. de Purg, Virchow's *Archiv*, Band viii., p. 301. Marfels, Moleschott's *Untersuchungen zur Naturlehre*, etc., Band i., p. 61. Lorange, *Quomodo ratio Cellularum alb. et rub. mutetur*, etc., *Diss. inaug.* Regiomont, 1856.

in the splenic artery, 1: 2,260; in the hepatic vein, 1: 170; and in the portal vein, 1: 740.

Several kinds of colourless morphological constituents can likewise be distinguished in the blood of the Frog* (fig. 74, *a*); namely, the ordinary amœboid cells, and the so-called granule cells, filled with highly refractile granules. The former (fig. 74) exhibit more, the latter less lively changes of form, associated in freshly drawn blood with locomotive movements, and likewise take up into their interior milk globules and particles of colouring matter.† Preyer‡ saw portions of the red blood corpuscles of extravasated blood in Amphibia taken up by white blood corpuscles, and thus explained the nature and mode of occurrence of the bodies that were previously called blood-corpuscle-holding cells. When acted upon by induced currents, and the discharges of voltaic electricty, these cells become round,§ just as occurs, according to Kühne, in amœbæ when irritated. Golubew showed that the cells of the frog, after having been made to contract by the application of a stimulus, recommence their movements. The character of these movements, however, is no longer the same as before the irritation; for, whilst the processes are in the first instance conical and finely pointed, on the recommencement of the movement after excitation they are more rounded, as well as shorter and broader, are quickly protruded, and are again withdrawn, to reappear in the immediate proximity; so that a kind of undulation runs round the corpuscle (fig. 74, *b*). After a short time, either the original character of the movement reappears, or the corpuscles expand on the recurrence of movements, into a flat disk. When in either of these phases, increased strength of excitation immediately causes the corpuscle to reassume the spheroidal form (fig. 74, *c*).

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* Rindfleisch, *loc. cit.*, p. 21. Kneuttinger, *loc. cit.*, p. 10, *et seq.* Golubew, *Sitzungsberichte der Wiener Akademie*, Band lvii., p. 555.

† Recklinghausen, Virchow's *Archiv*, Band xxviii., p. 185; *Die Lymphgefässe und ihre beziehung zum Bindegewebe.* Berlin, 1862, p. 22.

‡ *Loc. cit.*, p. 423.

§ Neumann, Reichert and Du Bois' *Archiv*, 1867, p. 31. Golubew, *loc. cit.*, p. 555.

After the continuous application of strong shocks the white corpuscles become destroyed, molecular movements occur in the swollen cells, or they are ultimately reduced to disks, and discharge their granules. A great number of these cells can be observed in an isolated condition if a drop of blood, recently obtained from a Newt or Frog, be brought upon a glass cover placed over a moist cell, and the drop, whilst freely dependent, allowed to coagulate. It is soon observable, when the zone of serum extends beyond the limits of the clot, that in this zone, in consequence of an active migration from the coagulum, numerous amœboid cells are present, and that they have accumulated on the surface of the coagulum.

Sclarewsky* has discussed this phenomenon of the migration of the white blood corpuscles from the coagulum at considerable length, as it may be observed in blood coagulated in capillary tubes. The above-mentioned simple experiment is far better adapted for the isolation of the cells for microscopical observation, and the investigations which can thus be made into the details of the migration of the individual cells renders it clear that the individual movement of the cells is the chief, if not the exclusive, cause of their emigration. The causes which must be admitted for the movements leading to this migration are still to be ascertained.

Besides these migrating cells a few small colourless structures, presenting the appearance of free nuclei, occur in the blood of the Frog at all periods of the year; lastly, we meet, in the blood of the frog, with the fusiform cells, first exactly described by Von Recklinghausen,† which, however, vary in number with the period of the year, being especially abundant in spring. They possess a bright homogeneous cell substance, and a granular oval nucleus.

Von Recklinghausen, who has acquainted us with the remarkable fact that if the freshly drawn blood of the Frog be preserved in moist air, after a short time an active process of cell formation takes place in it, which ultimately leads to the formation of red blood corpuscles, has also furnished some

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* Pflüger's *Archiv*, 1868, p. 660.

† Max Schultze's *Archiv*, Band ii., p. 137.

description of the intermediate forms that may be observed. Sclarewsky* and Golubew† have also been lately occupied with the investigation of the intermediate forms between the white and red blood corpuscles. From the statement of these authors it is to be concluded that the pale cells, which otherwise resemble red blood corpuscles, occurring in the blood of the Frog, and described by earlier observers, are to be regarded as amongst these intermediate forms.

From the facts just mentioned, we are directly conducted to the difficult questions of the origin and regeneration of the organised constituents of the blood.

Development of the Blood Corpuscles.

The first coloured blood corpuscles in the fowl originate contemporaneously with the formation of the first vessels in the germinal area,§ or in the vascular area and *area opaca*,‖ and they either detach themselves from the walls of the vascular spaces (Afanasieff), hanging together in isolated groups (blood islands, Wolf and Pander), or they may originate, according to the view of His, in the form of groups, from large masses of protoplasm in the walls of the vessels, and at a later period burst into their lumen. Soon after the coalescence of the vessels with the heart, these primordial blood corpuscles, which are lying ready to be borne onwards by the current, are floated off either separately or in groups (His). The primordial blood cells exhibit numerous processes and outgrowths (His). Moreover, the coloured blood corpuscles circulating during the later periods of intra-oval life exhibit numerous forms attributable to fission, which have been described and depicted by Remak.¶

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* *Centralblatt für die medicin. Wissenschaften*, 1867, p. 865.

† *Loc. cit.*, p. 566.

‡ Wharton Jones, *Philosophical Transactions*, 1846. Hensen, *loc. cit.*, p. 263.

§ Afanasieff, *Sitzungsberichte der Wiener Akademie*, Band liii., p. 560.

‖ His, *Untersuchungen über die erste Anlage des Wirbelthierleibes*. Leipzig, 1868, p. 95.

¶ *Untersuchungen über die Entwickelung der Wirbelthiere*, Berlin, 1855, p. 164 ; Müller's *Archiv*, 1858, p. 178.

In the tail of young tadpoles the newly formed vessels are found to be filled with peculiar, short, compressed, fusiform bodies, flattened on two of their sides, which present a very light yellow tint, and contain numerous yolk granules, but are otherwise homogeneous.

In addition to these primary cells there appear, it would seem, concomitantly with the progressive development of the intestinal tract, a constantly increasing number of white corpuscles. The number of the cells filled with yolk granules, on the other hand, gradually diminishes. We soon after meet with the intermediate forms already described as existing in adult animals, together with coloured blood corpuscles of the form ordinarily present in the blood of the Frog.

In Mammals there may be observed in the blood of the embryo, at an early stage, nucleated coloured blood corpuscles in process of fission. At a later period these forms are less abundant, in accordance with the progressive development of the embryo and of the spleen in particular (Kölliker), and we meet with numerous white corpuscles in the blood of the liver, which become metamorphosed into coloured nucleated blood corpuscles. Up to a certain period of embryonic life only nucleated red blood corpuscles are present in the blood (Kölliker). The non-nucleated first appear at a later period, their relative number then undergoing a constant increase. According to Kölliker, non-nucleated corpuscles are not present in the blood of fœtal sheep measuring three and a half inches in length; in those of nine inches long they are but seldom found, whilst they constitute the majority in fœtuses that are thirteen inches in length. According to Robin,† in human embryoes measuring thirty millimeters, about one half of the total number of blood corpuscles are destitute of nuclei; a few nucleated corpuscles are still discoverable in embryoes of the fourth month, and even at still later periods.

As has already been mentioned, the red blood corpuscles can

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* Kölliker, *Zeitschrift für rationelle Medicin*, Band iv., p. 112; *Gewebelehre*. Leipzig, 1867, p. 637. E. H. Weber and Kölliker, *Zeitschrift für rationelle Medicin*, Band iv., p. 160.

† *Journal de la Physiologie*. Paris, 1858, p. 288.

be regenerated in large numbers in the blood of adult animals, and this is accomplished at the expense of the white corpuscles, as was demonstrated in the case of the frog by V. Recklinghausen, and still more recently again by Golubew. Fission of the red blood corpuscles in adult animals has only been observed in a few rare instances.

Whether the colourless corpuscles always undergo multiplication within the blood itself, and by what mode of cell genesis they multiply, are still open questions. It is certain that a large number of white corpuscles are added to the blood, not only during the period of development and of growth of the animal organism, but also throughout life, by the agency of the lymph current, the corpuscles of this current originating in localized germ-producing organs, situated external to the blood (lymphatic glands).

If the continual addition of such young cells had only as an object the supply of material for the regeneration of the red blood corpuscles, it would demonstrate that the latter are very unstable structures, structures in which rapid metamorphoses take place. Independently, however, of the circumstance that it is possible the white corpuscles themselves undergo disintegration in the blood, we know as a fact that they migrate from the interior of the vessels into the tissues, and that they participate in effecting certain plastic processes in these tissues; on the other hand, up to the present time we are acquainted with only two regularly recurring processes, in one of which—menstruation—there certainly occurs, whilst in the other—the preparation of bile*—there very probably occurs the destruction of a large number of red blood corpuscles.

Moreover, the observations on the disintegration of the red blood corpuscles may here be alluded to, that have been described as taking place in the formation of pigment in the spleen, in the blood-corpuscle-holding cells of the spleen (*vide* spleen), and of the medulla of the bones; but in regard to the period of the occurrence of which during life nothing is at present known.

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* Kühne, *Physiologische Chemie*, p. 88.

Forms that may be supposed to be transitional between the white and the red corpuscles contained in the general mass of the blood of Mammals have however been described by Erb* under the term of "granular blood corpuscles," appearing in particular after artificial losses of blood.

Kölliker† adverts to the fact that he long ago found similar forms in the blood of the young sucking mouse. The mode in which they originate from the nucleated white corpuscles, and the stages of their conversion into the ordinary form of the red blood corpuscles, still require to be systematically followed out. In the blood of leucæmic patients nucleated red blood corpuscles are frequently to be found presenting the appearance of the nucleated embryonic blood corpuscles of Mammals and of Man.

Reference may here also be made to the statements advanced respecting the presence of red corpuscles in process of development in the pulp of the spleen. (See the chapter on the Spleen.)

In the last place, attention has very recently been directed by Neumann‡ to the nucleated red corpuscles constantly present in the medulla, and especially in the red medulla of bones (Man, Rabbit); and Bizzozero§ has corroborated the observations of Neumann in the case of Man, the Rabbit, and the Mouse. Both inquirers describe a complete series of transitional forms existing between the white nucleated and the non-nucleated red blood corpuscles, and associate the marrow of the bones consequently with the development of the blood. Still further communications on this function of the bony marrow have just been made by Hoyer.‖

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* Virchow's *Archiv*, Band xxxiv., p. 138, Taf. iv.

† *Gewebelehre.*

‡ *Centralblatt für die medicin. Wissenschaft. Jahr.*, 1868, p. 689; and *Archiv für Heilkunde*, 1869, p. 640.

§ *Centralblatt*, 1868, p. 881; and 1869, p. 149.

‖ *Centralblatt*, 1869, pp. 244 and 257.

CHAPTER XIV.

THE SALIVARY GLANDS.

By E. F. W. PFLÜGER.

§ 1. General Plan of Structure.—The salivary glands represented by the parotid, submaxillary and sublingual glands, when examined with the naked eye, appear to be rounded or polygonal yellowish-white masses, flattened by mutual pressure, and opening by hollow peduncles into a common excretory duct. The gland, in each instance, consists of a tube branching frequently in a tree-like manner, and lined throughout by a layer of epithelial cells. The numerous terminal branches, named alveoli, are lined by large tesselated epithelium, whilst the other portions are invested either with columnar or small tesselated epithelium, and present a clavate form, being arranged like grapes on the principal excretory duct. The salivary glands consequently belong to the group of acinous glands. The alveoli, however, with their secondary and tertiary processes, must not always be regarded as possessing the form of a berry, since they not seldom appear to be quite cylindrical, or only slightly contracted, where they spring from the trunk. The number of alveoli belonging to one of the smallest excretory ducts is so large that they lie tightly compressed and flattened in a polygonal manner against one another, leaving only a very small space for interstitial tissue.

The Alveoli.—If a section of the tubes measuring 0·030 millimeter in diameter be made, a canal and a wall may be distinguished. Even in glands hardened in alcohol it may easily be perceived that in the somewhat larger alveoli the

cavity is of very variable calibre, and may attain the mean diameter of a salivary cell, but may be also both extraordinarily fine (1—2 μ) and several in number in one and the same alveolus. The central canal gives off, as I have found, in conjunction with Mr. Anton Ewald, student in medicine, extremely fine tubuli (salivary capillaries), which penetrate between the salivary cells and also between the tunica propria and the epithelial cells; so that these, like the cells of the liver, are surrounded by tubuli that can be injected with Prussian blue, and appear to proceed from one alveolus to another. The parietes of the tubes, composed in general of a single layer of cells, are invested externally by an extremely fine, and when fresh, completely structureless membrane, called the membrana propria. The existence of this may be demonstrated by macerating the fresh submaxillary gland with distilled water, when the membrane becomes raised from the epithelium, often to a considerable distance, in the form of a hyaline vesicle. Recently the presence of a membrana propria in glands generally has been called into question, and especially by Schlüter,* in the case of the salivary glands. In order to exhibit it I would recommend the pancreas of the rabbit to lie for four days in iodized serum of a light sherry colour, and subsequently for two days in five cubic centimeters of diluted chromic acid, containing one-fiftieth per cent. By an action that is clearly of a digestive nature, the epithelial cells are in part detached, and obviously lie in a wide hyaline sac which they by no means fill. This appearance will incontestably demonstrate the existence of a membrana propria, forming a closed and continuous membrane.

A question of a totally different nature is whether this membrane may be regarded as being composed of flat cells fused or coalesced together. According to Boll† and Kölliker, it is composed of anastomosing connective-tissue cells that form a reticulum in which the alveolus lies as in a cavity of trellis or wicker-work. However plausible this view may appear on *à priori* grounds, there are facts which can scarcely

* *Disqisit. Mic. et Phys. de Gland. Salivar. Vratisl*, 1865; *Inaug. Diss.*

† Franz Boll, *Ueber den Bau der Thränendrüse im Archiv f. Mikroskop. Anatomie*, Band iv., 1868, p. 146.

be brought into unison with it. Thus, (1) on examination of the membrana propria in fresh preparations, I have never been able to distinguish a nucleus, although I tested for it with dilute chromic acid, which causes the nuclei of the epithelial cells to come into prominent relief, and although the quadripolar flattened cells regarded by Boll and Kölliker as constituents of the membrana propria frequently contain a very brilliant large nucleus, which, according to Boll, may be round and very thick. (2) The vesicular elevation of the membrana propria from the salivary cells, consequent upon diffusion, presupposes a continuous membrane, which in fact comes into view, whilst it is impossible to see any reticulum. (3) The small quadripolar cells of the reticulum so rarely occur in rabbits that they are by no means sufficient to furnish an investment to all the alveoli. (4) The quadripolar cells are unquestionably connected with the epithelial cells by means of processes, and cannot consequently be regarded as connective tissue cells, a point, into the consideration of which it will be hereafter necessary to enter. The view entertained by Boll and Kölliker has not, consequently, at present received adequate confirmation.

In the next place, as regards the contents of the alveoli. These consist of cells filled with numerous granules, so that the gland substance appears black by transmitted light, rendering it impossible to distinguish either the cell contour lines or the nuclei. Such are the appearances presented by perfectly fresh preparations made from the gland whilst still warm and almost living, if moistened with the aqueous humour. In diluted chromic acid, containing one-fiftieth per cent., the greater part of the granules quickly dissolve, whilst the alveolus becomes transparent, and presents the most beautiful mosaic of cells. For this experiment the submaxillary glands of the rabbit are admirably adapted. Every cell is rendered polygonal by mutual compression, and presents sharply defined bright double contours. For the most part they only form a single layer, which lines the central canal of the gland, and is differentiated from this by a sharp contour line. In most animals the membrana propria is easily elevated. The cells adhere very strongly to one another, so that after being detached from the

membrana propria they still hang together in small groups. It is noteworthy in regard to the size of the epithelial cells, that as a general rule those contained in the same alveolus are of nearly the same size. But if we compare those belonging to different alveoli, they are found to be of very different dimensions. It is possible that the small epithelial cells may belong to alveoli of smaller diameter. There may, however, be found all the transitional forms between the two, so that we are here dealing only with the same gland substance in different stages of development. This remark applies also to adult animals.

If we now proceed to examine with more minuteness the salivary cells of the alveoli, I must in the first place observe that they appear to be invested by a membrane both towards the lumen of the tube and where they are in apposition with each other. It is important to observe that the double contours of two salivary cells in contact with one another, are not always perfectly distinct, as though at some points there existed a still more intimate union between them. The protoplasm of the salivary cells is tenacious, finely granular, and frequently striated. A cell of this kind may give rise to the impression that its protoplasm is composed of innumerable extremely fine fibrils. The average size of the salivary cells is 0·014 millimeter in diameter. The largest epithelia of this kind with which I am acquainted, I have found in certain alveoli of the salivary glands of the Ox.

An extremely pale spherical nucleus is to be found in the interior of the protoplasm in all fresh specimens, and even in those that have been moistened with diluted acids. After the action of the acid has been long continued, it becomes highly refractile, and presents a dark and sometimes double contour line. It then gradually shrinks, and applies itself as a flat disk to the wall of the cell, which frequently renders its recognition a matter of difficulty. The cell nucleus lies eccentrically to the salivary cell and alveolus, and immediately beneath the membrana propria. Its average size in the fresh condition, after being brought into view by dilute acids, amounts to 0·306 millimeter. The most remarkable peculiarity presented by the nuclei of the cells, when fresh, is that they give off an extremely delicate fibre (fig. 75), which often penetrates that surface of the salivary cell

which is in contact with the membrana propria. I have seen these caudate nuclei in perfectly fresh specimens. The submaxillary gland of the rabbit or pig is best adapted for their demonstration. The existence of the processes of the nuclei has been corroborated by C. Otto Weber, as well as by Boll, whilst by Kölliker and Heidenhain, though undoubtedly incorrectly, it is denied. The latter,* it is remarkable, has himself drawn a thick process, attached with such remarkable distinctness to the nucleus of an isolated salivary cell, receiving as it leaves this a sheath of the cell membrane, that, upon the

Fig. 75.

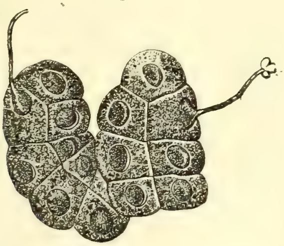

Fig. 75. Isolated alveoli of the Rabbit, exhibiting processes. Magnified 480 diameters.

ground of this positive observation alone, I should draw the conclusion that the process is frequently not seen in connection with the cell, because it is destroyed in putting up the preparation. The nuclear process appears to be hollow, since it often discharges a large quantity of tenacious material, which clearly proceeds from the nucleus. In consequence of the nuclear process leaving the cell, it gives the latter the appearance of being stalked, as has been seen by Schlüter, myself, Gianuzzi, Boll, and Kölliker. According to the descriptions given by Schlüter and myself, the cell processes are often of great length, branch, coalesce (Schlüter), and support the alveolar cells like berries.

There is never more than one nucleus in each salivary cell.

* R. Heidenhain, *Studien des physiologischen Instituts zu Breslau*, 1858, Taf. iv., fig. 13 *x*.

Occasionally, indeed, there appear to be more, but in such cases there is always a doubt whether the line of division between two adjoining cells is perceptible.

According to Heidenhain, there are two kinds of salivary cells, of which one contains mucus, but no albumen; the other albumen, but no mucus. The former he denominates "mucous-cells," the latter "albuminous-cells." Both are glassy, transparent, and delicately striated; the latter are, in addition, finely granular. Where mucous cells predominate, as in the submaxillary gland of the dog, cat, ox, and sheep, they may perhaps represent the young condition of the albuminous cells. In the rabbit, at least in the submaxillary gland,* no mucous cells are, according to this observer, to be found.

Besides the points already described, there still remains to be noticed a structure, first mentioned by Gianuzzi, and to which he has applied the term semi-lunar body.†

When sections are made of hardened salivary glands, there appears here and there a concavo-convex lenticular lamina, usually of very small thickness, which adheres intimately to the alveolus surrounding the salivary cells that lie in its cavity, and presents, on section, a semi-lunar form But inasmuch as, on investigation of fresh glands, I was never able to see the semi-lunar body, and found that even in rabbits it eluded my observation, I was inclined, since this structure is only demonstrable in those animals which have mucous cells, to regard the semi-lunar body as an artificial product, and as originating in the *post-mortem* formation of a mucous vesicle, compressing the cell protoplasm towards the wall. And it is remarkable that, according to the recent investigations of Heidenhain, the submaxillary gland of the dog, when the mucus is withdrawn from it, no longer presents the demi-lune, but resembles the same gland in the rabbit.‡ The elimination of the mucus is effected by exciting the gland to

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* See Heidenhain, *loc. cit.*, p. 6.

† S. Gianuzzi, "On the effects of acceleration of the blood currents on the secretion of Saliva;" *Ber. d. K. Sächs Ges. d. wiss. Math. Phys. Classe, Sitzung vom* Nov. 27, 1865.

‡ Heidenhain, *loc. cit.*, Taf. ii., fig. 5.

react through the nerves for many hours, whereby the mucus and the mucus-forming materials are consumed.

Later inquirers do not agree with me in my opinion regarding the demi-lune; nevertheless, they completely justify it, by each one giving a different interpretation of its nature. C. Ludwig and Gianuzzi ascribed to it a laminated structure, and described the blackening it underwent from the action of perosmic acid, and the reddening with carmine. They were unable to see nuclei distinctly. Boll and Kölliker described the "half-moon" as composed of connective tissue, which, firmly adherent to the alveolus, represents the cells constituting the reticulum already referred to. Heidenhain maintained that the demi-lune was formed by a layer of young epithelial cells, destined to supply the place of those salivary cells which were undergoing distintegration. I believe this view to be not an unreasonable one, for inasmuch as in the submaxillary gland of the dog the protoplasm of the mucous cells is scarcely, if at all, tinted with solutions of carmine, whilst the small nuclei lying at the periphery, as well as the numerous superimposed long cell processes running outward, are deeply stained, we have a sufficient explanation of the occurrence of a complete marginal zone in the alveolus. But since the term "demi-lune" can possess such different significations, it is better to avoid its use entirely.

§ 3. The Excretory Ducts.—In the interior of the gland, besides the structures already described, are tubes often of considerable size, and lined with cylindrical epithelium, to which the name of excretory ducts is applied. Close investigation shows that they must possess great functional importance. As evidence of this, I would first remark that if a dog be killed as rapidly as possible, and fine sections be prepared from the submaxillary gland, transparent drops may be seen exuding from the columnar cells lining the excretory ducts, and some of these having already become detached, lie in the lumen of the tube, appearing in the form of round, sharply defined, clear spherules. These unquestionably proceed from the cylindrical epithelium. But inasmuch as drops, presenting precisely the same appearances, are found in freshly secreted saliva, that has

been caused to flow by irritation of the gland, it would appear highly probable that these cylindrical epithelial cells also belong to the secretory apparatus. Anatomical examination tells still more strongly in favour of the importance of these structures, since it then appears that the thickness of the wall of the duct, as we advance towards its peripherical distribution, instead of, as might be expected, diminishing, undergoes material increase. The thickening of the wall is, in general, occasioned by the elongation of the cylindrical cells, which, however, never form more than a single layer. Besides this, the wider ducts exhibit more or less strongly marked outgrowths, lined with the same epithelium. If the ramifications of the ducts be traced in a peripherical direction, fine passages are at length met with, having a diameter of 0·010 millimeter, possessing the same epithelial lining as the larger ones, and, if I am not mistaken, terminating in blind extremities; these are the secretory tubules—that is, the capillaries of the salivary ducts having the same tenuity as the biliary capillaries, and leading to the alveoli. In a word, these excretory ducts, or *salivary tubes*, possess diverticula of various form. Not unfrequently they form loops or bend suddenly.

If we now proceed to the study of the characters of the

Fig. 76.

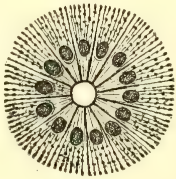

Fig. 76. Transverse section of a fresh salivary tube in diluted chromic acid of one-fiftieth per cent. Magnified 480 diameters.

columnar epithelium, the cells will be found to possess an average diameter of 0·004 millimeter, and to be of very variable length. The cylindrical epithelial cells are so well defined at their points of contact with each other, and on their free surfaces directed towards the interior of the tube, that they appear to possess a membranous wall; and these walls, towards

the lumen of the tube, are united into a highly refractile continuous layer, the cells being here intimately adherent. They are, however, strongly adherent elsewhere—to so great an extent, indeed, that when in the fresh condition it is impossible to isolate them. If the surface of the tube be examined, a beautiful mosaic of cells comes into view, the transverse section of the cells being for the most part completely filled by a well-defined nucleus. The cell contents, when a freshly made transverse section of the salivary duct of a dog is examined, appears to be perfectly hyaline. This animal is well adapted for the purpose, because the toughness of the gland (submaxillary) permits fine sections to be made of it whilst still warm, after removal from the body. The most remarkable feature of these cylindrical epithelial cells is presented by the surface turned from the canal, and which is immediately in contact with the membrana propria. From this spring a large number of extremely fine varicose hairs, quite a bunch or pencil of such hairs proceeding from each cell. The surface of the tube composed of these cylindrical cells, always easily capable of detachment from the membrana propria, appears, on account of the equality in length of the several hairs, like a thick brush. These extraordinarily fine fibrils may be observed in any of the fluids in which the fresh gland can be properly examined. There may also be constantly seen, on focussing the surface of the salivary duct, fine points, which represent the optic transverse section of these varicose fibrils. For these reasons I am not disposed to regard these brushes as artificial products, which have originated by a splitting of the peripheric portion of the cells.

Whilst in most cells the fibres commence immediately below the nucleus, it may be observed in some preparations, in which the cells have been isolated in iodized serum, that a few fibrils take origin from a higher point in the interior of the cell. In many of these cylinders the body of the cell very constantly presents the appearance of being delicately transversely striated. In the greater number of instances, however, that portion of the cell which is next to the canal remains transparent. From preparations made with iodized serum, it can be shown that some of these cylindrical cells, in consequence of the smallness

or disappearance of their processes, and the assumption of a polygonal form, approximate closely to the flattened epithelium found in the alveoli. This similarity also extends to the cell contents and to the nucleus.

Besides these extremely fine processes of the columnar cylinder cells, resembling the fibrils proceeding from the axis cylinder of a nerve, others of greater thickness, and of high refractive power, may be observed to be given off from their sides. The significance of all these processes will be hereafter discussed at greater length.

Lastly, as regards the dimensions of the calibre of the tubes, it is found that they vary from a diameter of 0·030 millimeter or less to a size easily recognisable with the naked eye. The enlargement is essentially effected by increased diameter of the lumen, and to a less extent by increased length of the columnar epithelium. I have met with such canals in the interior of the glands of the dog, the lumen of which had a diameter of 0·1 millimeter or more.

Besides the salivary tubes, other tubes are found in the salivary glands, varying considerably in diameter, and lined by a small description of tesselated epithelium, that generally diminishes with the bore of the tube. These may be injected through the ordinary excretory ducts, as well as through the salivary tubes, and ultimately form by their ramifications passages which have only a diameter of 0·007 millimeter or less, and are lined by a very small-celled pavement epithelium. These passages constitute without doubt, excretory ducts proceeding from the alveoli, and form a stage in that developmental metamorphosis of the gland which exists even in the adult.

Whether the salivary tubes, which are continuous with these excretory ducts lined by pavement epithelium, communicate with the alveoli, and in what way this communication, if present, is effected, demands further investigation. I know for a fact that a mosaic of salivary cells may lie in immediate juxtaposition to columnar epithelium; but it is very rare for the canal of a salivary tube to be directly continuous with a canal which is lined with salivary cells. I am of opinion that the communication between the salivary tubes and the alveoli is effected by means of very fine passages (salivary capillaries).

The proper excretory ducts (Ductus Whartonianus, Stenonianus, etc.) are generally admitted to be lined by an epithelium, consisting of a single layer of short cylindrical cells. Boll, however, describes the epithelium as composed of tesselated cells. The wall is strengthened by fibres of connective tissue, with numerous elastic fibres and membranes, as well as by smooth muscular fibre cells.

§ 4. Distribution of Nerves in the Salivary Gland.—The nerve tissue of the salivary glands consists of ganglion cells and fibres. The latter are composed both of medullated, which constitute the greater number, and of pale nerves.

Three different kinds of pale nerves may be distinguished.

a. Fasciculi of extremely delicate transparent fibres, presenting the characters of axis cylinders, and invested with a sheath of connective tissue, containing nuclei. Were it requisite to adduce any proofs of the nervous nature of these fasciculi, it might be pointed out that these pale fibres form from time to time large fusiform varicosities, consisting of nerve medulla, characterised by its double dark contour. The pale fibre between two such varicosities differs in no respect from that lying in their immediate proximity. The above feature, however, renders it probable that these pale fibres conceal a thin layer of nerve medulla between the axis cylinder and the sheath. At the same time, neither a special investing sheath nor nuclei can be demonstrated around the individual primitive fibres, as indeed follows from what has been above stated, and these consequently, in the fresh condition, possess the appearance of naked axis cylinders.

b. A second kind of pale nerve fibre found in the salivary glands I shall denominate gelatinous fibres. They consist apparently of bands of finely granular protoplasm, lying in a sheath of connective tissue, in which are nuclei, and presenting exactly the same appearance and behaviour as the protoplasm of the large ganglionic cells of the glands. Such gelatinous fibres may be observed to leave the ganglion cells, and hence are unquestionably of a nervous nature. They are probably composed of fasciculi of extremely fine varicose fibrillæ, which, lying in close apposition, give the impression of a finely granular,

somewhat striated protoplasm. These fibres present the same appearance as the so-called protoplasmic processes of the nerve cells of the cerebrospinal organs.

c. A third kind of pale fibre is composed of bundles of somewhat tougher, more highly refractile, very fine (0·0005 millimeter) fibrils, which likewise lie in a tube of connective tissue containing oval nuclei. These are liable to all the objections that have been raised on various sides against the nervous nature of the fibres of Remak.

Fig. 77.

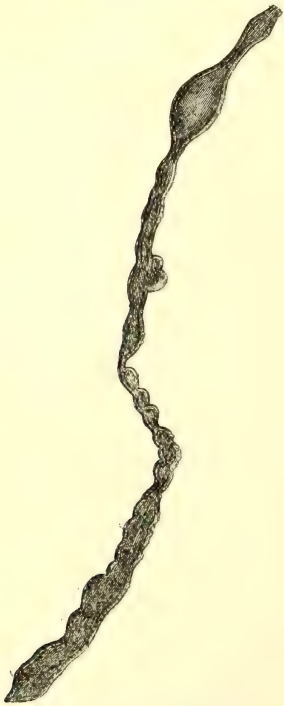

Fig. 77. The preparation was taken from the submaxillary gland of the Ox, and was blackened with perosmic acid. Magnified 590 diameters.

The medullated fibres, which are present in extraordinary numbers in all parts of the salivary glands, and of all sizes down to those of only 0·0015 millimeter in diameter, present

a series of very remarkable peculiarities. In the first place they have such delicate and pliable sheaths, that they sometimes appear to be destitute of them. In accordance with this, varicosities form in the coarser trunks, as in the fibres of the brain or spinal cord (see fig. 77), where, however, they become still larger, and form more easily than amongst these. On account of the extraordinary delicacy of the sheath these fibres tear with remarkable facility, and pour forth their contents in the form of myelin drops, which rapidly become stained of a blue-black colour by osmic acid, like these nerves themselves.

A second peculiarity of the medullated glandular nerves is exhibited in their mode of division, the division occurring so frequently as to have been seen by almost all observers. According to my own observation, the number of divisions increases in a most unusual manner towards the periphery, so that almost feathery medullated primitive fibres lie between the alveoli, and give off branches in all directions.

If we now proceed to the consideration of the terminal organs of the nerve fibres, we must first discuss the relations these bear to the proper tissue of the gland. The salivary tubes, with which we shall best commence our description, are accompanied by numerous bands of medullated nerve fibres of very various size. Many are in the most intimate relation with the tubes, as is shown in the accompanying figures. In one instance the specimen was fresh (fig. 78), in another it was stained by maceration in perosmic acid (fig. 79).

These nerves, as seen in figs. 78 and 79, perforate the membrana propria, and then break up into a number of fibres, which become finer by further subdivision, and wind around the outside of the columnar epithelial cells, to form a sub-epithelial plexus, which demands still closer examination. The fibrils lying on the membrana propria are pale and soft, and give the impression of naked axis cylinders. But that they are accompanied for some distance by the nerve medulla is recognised by the blackening of the osmic acid preparations around the termination of the thicker primitive fibres. The axis cylinders running on the membrana propria branch ultimately into the finest possible varicose fibrils, which have precisely the same characters

Fig. 78.

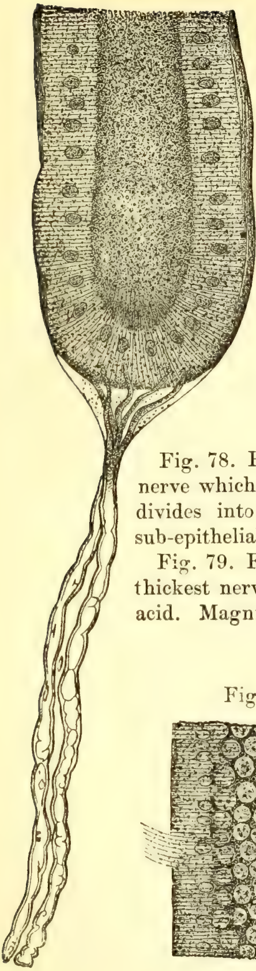

Fig. 79.

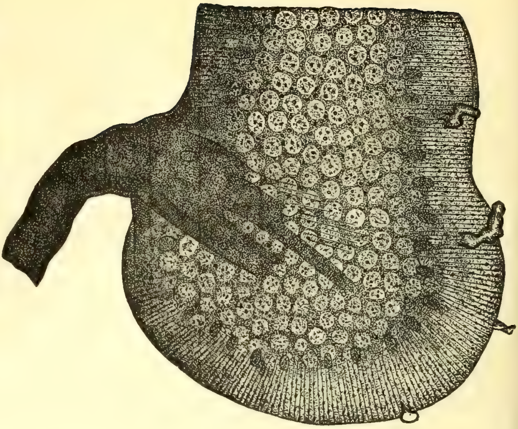

Fig. 78. Fresh specimen. From the Ox, exhibiting a medullated nerve which penetrates the membrana propria. The axis cylinder divides into branches upon the membrana propria to form the sub-epithelial plexus. Magnified 590 diameters.

Fig. 79. From the Ox, showing the termination of one of the thickest nerve fibres at a thick salivary tube blackened by perosmic acid. Magnified 590 diameters.

Fig. 80.

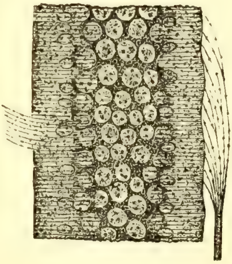

Fig. 81.

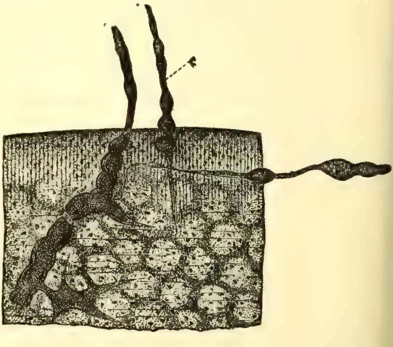

Fig. 80. Showing an axis cylinder breaking up into fibrils which are continuous with the fibrils of the columnar epithelium. Magnified 590 diameters.

Fig. 81. From the Ox, showing medullated and in part varicose nerves blackened by perosmic acid, which branch in the sub-epithelial plexus, and one of which (*n*), can be distinctly traced into the processes of the columnar epithelial cells. The preparation exhibits a marginal portion of the surface of a salivary tube. Magnified 800 diameters.

as the fibrils which emerge and join them from the columnar epithelial cells. It is frequently observable that the last ramifications of the axis cylinder are continuous with these fibrils; and that the columnar cells thus represent the continuations of the finer and the finest medullated nerves with the sub-epithelial plexus is frequently capable of direct proof, as appears from an examination of fig. 80. We may even succeed, though rarely (fig. 82), in effecting the complete isolation of all parts, and in thus showing the continuity of the medullated nerves with the processes of the columnar cells. It may thus be rendered evident that these fine processes are in direct continuity with the axis cylinder, from which they do not in any respect differ. At the same time it may be remarked that the axis cylinder of the

Fig. 82.

Fig. 82. From the Rabbit, exhibiting a medullated nerve, becoming continuous with an axis cylinder which passes directly into the process of a cylinder cell, and directly opens into the columnar cell. Magnified 590 diameters.

afferent nerves appears to be thicker than the fibrillar processes of the columnar cells, which must consequently be regarded as continuations of the fibrillæ of the axis cylinder. After the nerve has penetrated the membrana propria of the salivary tube, the axis cylinder either immediately terminates, or does so after it has first run for some distance upon the membrana propria; in

the latter case it runs between this and the fibrillar processes of the columnar epithelial cells.

When we consider the incredibly large supply of nervous fibrils that lies beneath the membrana propria, the question of the object of this abundance naturally suggests itself. After studying with greater exactitude the laws of the growth of glandular epithelium, we shall find that a completely satisfactory solution of this question may be attained. I shall treat of this point, however, at a later period. I would only mention here that numerous young salivary cells develop from every columnar cell, with its fibrillar processes, and that each of these must again have its proper nerves. This is true also in the case of the adult animal. From the almost imperceptibly fine fibrils of the columnar cells the fibres of the epithelium cells of the alveoli proceed, which we shall now subject to a careful consideration.

Two kinds of nerve termination are to be distinguished in the alveoli :—

I. The most important is that of the medullated primitive

Fig. 83.

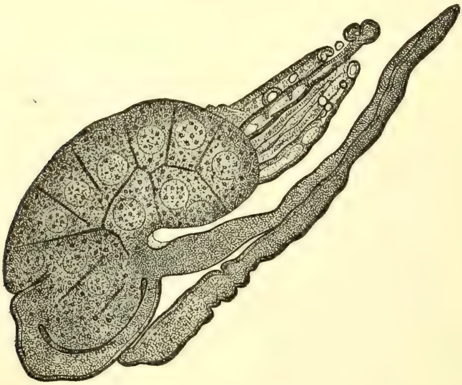

Fig. 83. From the Ox. An alveolus with the terminations of medullated nerves which have been blackened by perosmic acid. Magnified 590 diameters.

fibres. These branch very frequently between the alveoli, apply themselves to the membrana propria, and usually give off at the point where they penetrate it several branches, which run for

some distance on its outer surface to the nearest epithelial cells, in order to penetrate over these into the alveolus (fig. 83). The nerve becomes blackened by perosmic acid up to the point where it perforates the membrana propria; at this point the

Fig. 84.

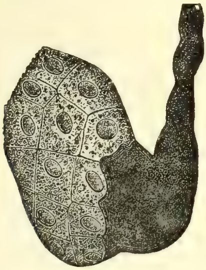

Fig. 84. From the Rabbit. Medullated fibre blackened by perosmic acid. Magnified 500 diameters.

medulla appears to cease (figs 84 and 87). That the membrana propria is perforated is shown in the most striking manner by the circumstance that the continuity of the medullated and

Fig. 85.

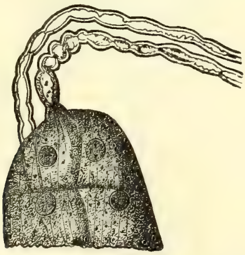

Fig. 85. From the Rabbit, after maceration in iodized serum, showing the termination of a medullated nerve in an alveolus. From the submaxillary gland. Magnified 590 diameters.

frequently very thick primitive fibres with the salivary cells may often be easily demonstrated. I have seen this occur in a great variety of modes, and in the clearest manner in the

salivary glands of the ox and rabbit (submaxillary and parotid glands) (figs. 87 and 88).

Fig. 86.

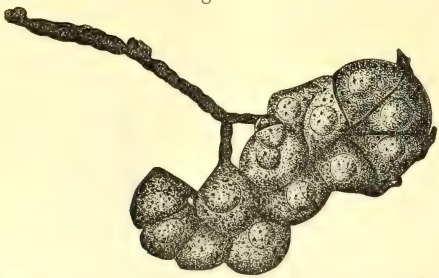

Fig. 86. Termination of a branching fine medullated fibre in the salivary cells of an alveolus. From the submaxillary gland of the Ox, the nerve blackened by perosmic acid. Magnified 490 diameters.

In completely isolated preparations (Figs. 86 and 88, A B) it may be observed that the white substance of Schwann ceases

Fig. 87.

Fig. 87. Termination of a medullated fibre of average thickness in the large salivary cells of an alveolus. From the submaxillary gland of the Ox. The nerve has been blackened by perosmic acid. Magnified 500 diameters.

as though suddenly cut off at a short distance from the salivary cells, and that the nerve appears as if adherent to the soft protoplasm of the epithelial cell.

If the point of attachment be examined with very high magnifying powers, it will be seen that immeasurably fine fibrils proceed from the nerve, which pass directly and without interruption into the fibrils of the protoplasm of the salivary cells. This appearance is most beautifully presented if the medullated fibre be deprived of its medulla by pressure. There then remains a pale fibre composed of extraordinarily fine

Fig. 88.

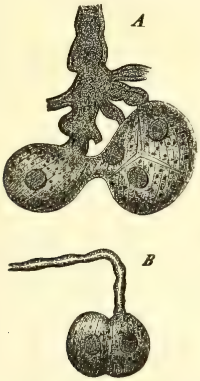

Fig. 88. Termination of medullated fibres treated with perosmic acid in isolated salivary cells. A, thick branched fibres distributed to large salivary cells ; B, fine nerves distributed to smaller salivary cells. From the submaxillary gland of the Rabbit. Magnified 590 diameters.

fibrils, which are directly continuous with the fibrillated substance of the epithelial cells. This character is especially important, because it constitutes a clear evidence of the absolute continuity and fusion of the axis cylinder and epithelial cell. As I have not seen any fibres blackened by perosmic acid upon the membrana propria, though both the blackening and the medulla may constantly be seen extending to epithelial cells in well-isolated preparations, I must conclude that ordinarily the mode of termination in the alveoli is that the nerve perforates the membrana propria, and enters directly into the superjacent salivary cells. The nerve medulla consequently terminates at the cell. That point of the salivary cell where the nerve enters is marked by a slight in-

crease in the transparency of the protoplasm, and this portion occupies a segment made up of from one-fourth to one-third of the spherical volume of the cell (fig. 88). I have not seen the nucleus in this segment, but in the remaining more darkly granular portion. The nerve tears across with remarkable facility at the point of its insertion, which appears to be extremely soft, and hence leaves no trace of the point at which it was attached to the cell. This may be reasonably attributed to the fact that the connection is only effected by means of the axis cylinder, which, whilst it is continuous with the semifluid protoplasm of the cell, undergoes no sudden interruption at this point. It is on this account impossible, without appropriate, though necessarily very slight, hardening with reagents, to bring into view the isolated fresh salivary cells, with their associated nerve fibres. It is not surprising that the medullated primitive fibres are sometimes very fine, sometimes very thick, when we know that the epithelial cells gradually increase to substantial structures, from minute nodules on extremely fine axis-cylinder fibrils. With their increase the size of the nerve also augments; it acquires a medulla, and becomes progressively thicker. It is this circumstance in part, and partly the fact already mentioned, that, on the application of pressure or other form of mechanical violence, the medulla separates from the dark-edged primitive fibres, whilst the axis cylinder breaks up into fibrils penetrating the protoplasm of the salivary cells, that forbids us any longer to regard the latter mode of nerve termination as peculiar.

Whether this holds for all pale nerve terminations found in the alveoli appears to me, from the stand-point obtained in the physiological experiment demonstrating that two kinds of nerves exert an action upon the gland, to be doubtful. There may in particular be found well-preserved long tubes, apparently composed of connective tissue, the wall beset with nuclei, continuous with the membrana propria of the aveoli, and containing one or more fine fibrils, that are lost in the gland vesicles. They rarely occur in comparison with the medullated fibres, but are more stable on account of their sheath, so that they alone can be seen in some of the modes

of preparation, on account of the fluidity of the medullated fibres.

II. On the mode of Nerve Termination effected by Multipolar Cells.—I have elsewhere described small pale cells (fig. 89) possessing numerous processes adherent to the alveoli, and for the most part smaller than the salivary cells. I regard these as nerve cells, and consider them as entering into communication, not only with the salivary cells, but also with the nerve fibres.

All later inquirers (Kölliker, Boll, Heidenhain) have with remarkable unanimity and with great precision described these multipolar cells as indifferent structures *forming a reticulum,*

Fig. 89.

Fig. 89. Multipolar nerve cell. From the Rabbit. Magnified 80 diameters.

and properly to be regarded as belonging to the connective tissue. According to Kölliker and Boll, these cells constitute the membrana propria, which I have already described.

The above-named inquirers silently assume that the opinion I hold of the direct continuity of these multipolar cells with the glandular epithelium by means of thick and anastomosing fibres is erroneous. Boll was unable to discover these communications, but refers to *apparent* connections, and is of opinion that the multipolar cells, with their intercommunica-

tions, in some instances closely resemble salivary cells, so that the possibility of a false impression is conceivable.

But as I am satisfied that I have seen the connection of the multipolar cells with salivary cells, I hold it to be my duty, especially on account of the importance of all that depends upon it, to prove this point with the most rigorous scientific accuracy. As I have more recently on many occasions observed such connection, I may remark that we are here engaged with the examination of completely isolatable cells, which communicate with one another by means of a thick anastomosis, and the two points of attachment of which may be seen in perfect profile (fig. 90, A B C). One of these cells is pale, striated, with many radiating processes, and with the body almost entirely filled with the nucleus (fig. 90, B). The other is round or slightly polygonal, with abundant granular protoplasm and a relatively small nucleus.

Fig. 90.

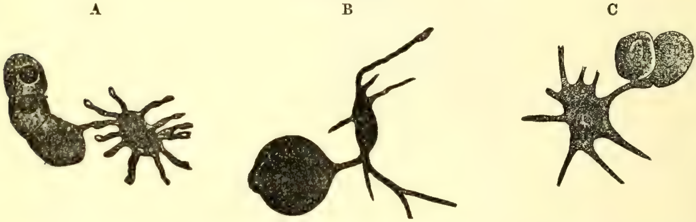

Fig. 90, A, B. Multipolar cells in connection with salivary cells. Magnified, A, 480, B, 590 diameters.

C. Peculiar cells with round thick processes, and containing refractile fat particles. Magnified 590 diameters.

As the observations were made upon rabbits, the fully developed salivary cells of which have so stereotyped an appearance, I regard it as absolutely impossible that I should have mistaken any other cell for a salivary cell. Moreover, I have actually seen the connection whilst the salivary cells in question were still adherent to others, and forming part of the characteristic mosaic (fig. 90, A and C).

It follows therefore that the multipolar cells cannot be connective tissue cells, as maintained by Kölliker, Heidenhain, and Boll; for the true salivary cell is an enlargement of a medul-

lated nerve. It cannot, consequently, give off any process which is a connective tissue fibre, or which is continuous with connective tissue cells; for between animal tissue and connective tissue substance there cannot be any continuity of substance.

Inasmuch as I am now satisfied that the multipolar cells are continuous through their processes with nerve fibres (fig. 89), it follows that they must either be modified epithelial cells or ganglion cells. Their continuity with nerve fibres does not decide the question, since the salivary cells also present this character under the most various modifications in common with true nerve cells.

There consequently remain, as means for determining the point, only analogy and anatomical structure. To whatever degree the multipolar cells may differ amongst themselves in their size and form, and in the characters of the nucleus and of the protoplasm, as indeed was observed by Boll, they nevertheless resemble nerve cells more closely than epithelium, as is shown by the fact that small ganglion cells have been admitted to occur amongst them by various observers, as by Henle and Krause. In the next place, in regard to the great variation that they present, it is important to remember that if the alveoli, as we have decisively proved, undergo continuous regeneration and disintegration, the nervous tissue must be subject to similar metamorphoses. The nucleus in some of these remarkable cells is round, as was also observed by Boll; and is at the same time transparent, and almost entirely fills the cell. This peculiarity is presented also by other peripheric ganglia, as the granules of the rods and cones of the retina, which unquestionably represent bipolar nerve cells. Moreover these cells exhibit a pale striated protoplasm, the fibres of which may be followed into the similarly striated, and in parts highly refractile, cylindrical processes. Such cells consequently, taken as a whole, exactly resemble, and would be held by all to constitute, ganglion cells.

Besides these, we find other cells with ellipsoidal or flat nuclei, which are partly round and partly present flat processes and membranous cell substance, and are quite transparent. Finally, there are still others, lying within the young alveoli

which possess granular soft protoplasm in sparing quantity, contain round highly refractile nuclei, and possess numerous cylindrical highly refractile processes. These are undoubtedly in an early stage of development (fig. 90, C). Even if these cells form a reticulum, this furnishes no evidence of their indifferent nature, since all ganglion cells are beyond doubt parts of the great network of animal tissue.

Lastly, even if, looking at the great variety of multipolar cells, it be admitted that we are here dealing with cells of different nature and attributes, it still appears to me that we have obtained a sufficient answer to one of the above alternatives, and that the multipolar cells must be regarded as small ganglion cells.

The mode of termination of the nerves here described I have termed that "effected by the means of multipolar cells," an expression which is only in accordance with fact, and to which, consequently, no objection can be raised.

The remarks hitherto made upon the relation of the nervous system to the salivary glands refer exclusively to the submaxillary gland.

At the same time I have convinced myself that the alveoli of the parotid gland enter into relation with strong medullated nerves in the same manner as has been just described in the case of the submaxillary gland. The parotid, moreover, as well as the sublingual gland possesses salivary tubes presenting similar structural features. Krause has demonstrated the presence of similar multipolar cells in the parotid, and I have also more recently found them in the sublingual gland. If we take into consideration the very similar structure that is thus exhibited by these glands, and the dependence of their activity upon the nervous system, we can scarcely hesitate to believe that a complete agreement prevails also in regard to the mode of termination of their secretory nerves.

As regards the sensory elements of the nervous system, W. Krause* has discovered a simple kind of Pacinian corpuscle, to which he has given the name of "Terminal Gland Capsules." In the majority of animals, however, they are rarely present.

* *Zeitschrift für rationelle Medicin*, Band xx., p. 60, 1849.

The structure of the larger ganglia which are found in the course of the nerve fibres and trunks still remains to be considered. The ganglion cells occur partly isolated and partly in groups which accompany the nerve cords for a considerable distance, or form roundish knots enclosed by a dense sheath of connective tissue. These knots attain the size of 0·060 millimeter and more. The nerve cells lying in their interior (fig. 91) have a diameter of 0·028 millimeter, with a nucleus of the diameter of 0·012, and a nucleolus of 0·002 millimeter in diameter.

We meet also with much smaller ganglion cells, which are not larger than salivary cells, with a diameter of or about 0·014 millimeter. The cells accumulated in one group do not mate-

Fig. 91.

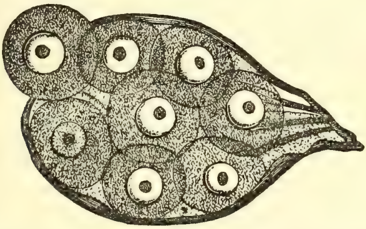

Fig. 91. Ganglionic knot from the submaxillary gland of a Rabbit. Magnified 480 diameters.

rially differ from one another in their general magnitude. The ganglion cells include a spheroidal or oval, transparent, delicate, but sharply defined nuclear vesicle, and when in their fresh state their protoplasm is very delicate and confusedly granular.

In the smaller forms the cell contents are sometimes rather more granular, but the nucleus is always as clear as water. The groups are constantly in connection with afferent and efferent nerve fibres. In some instances a single ganglion cell is found in the course of a fibre of Remak. It is remarkable that a large ganglion cell of this kind, having a diameter of 0·042 millimeter (see fig. 92), may contain several nucleoli; and, moreover, at the point of transition into the nerve fibre, may present a slight deposit of protoplasm, with several ganglionic

nuclei; and I desire especially to direct the attention of observers to this singular form of ganglionic substance. The relations of the ganglion cells of the gland are also deserving of special investigation, which will certainly bear on the physiological point of whether the sympathetic is distributed exclusively to the bloodvessels, or whether it does not stand in intimate relation to the secreting cells.

Fig. 92.

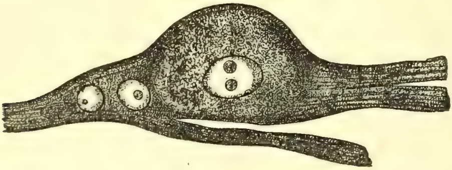

Fig. 92. Solitary ganglion cell with a deposit of nucleated ganglionic protoplasm. From the submaxillary gland of the Rabbit. Magnified 480 diameters.

§ 5. The Regeneration of the Glandular Epithelium.—I have already called attention, in my work on "The Termination of the Secretory Nerves in the Salivary Glands," to the alveolar-like small projections or bud-like processes of the so-called excretory ducts, and have there expressed the opinion that, both in the primary embryonal development of the gland, as well as in the adult, new salivary cells and alveoli develop from the salivary tubes. I am now in a position to describe the process with accuracy.

If the salivary tubes isolated by any of the ordinary modes, or sections of them, after the action of hardening agents, be carefully examined for the brush-like processes of the cylindrical epithelial cells, it is easy to observe that the fibrils in various salivary tubules, or even in separate sections of the same tube, may present a very different appearance. As a general rule, even with the highest powers, they appear as immeasurably fine varicose fibrils (fig. 76). But all conceivable intermediate or transitional forms may be met with, up to moderately thick fibres (0·001 millimeter) (figs. 93 and 94). In proportion as they increase in size they lose their soft pale appearance, acquire high refractive

power, which begins to be apparent at the free extremity of the cylindrical cells, and gradually extends towards that extremity to which the fibres are attached. The end of the fibre frequently

Fig. 93.

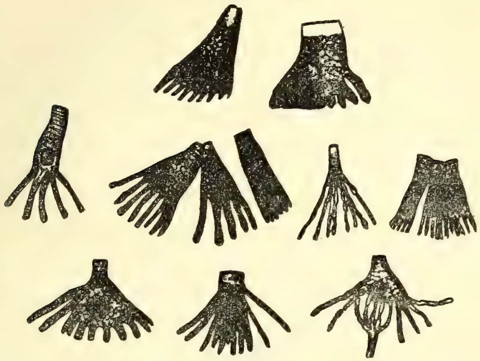

Fig. 93. Cells. From the submaxillary gland of the Rabbit, after maceration in iodized serum. Magnified 590 diameters.

Fig. 94.

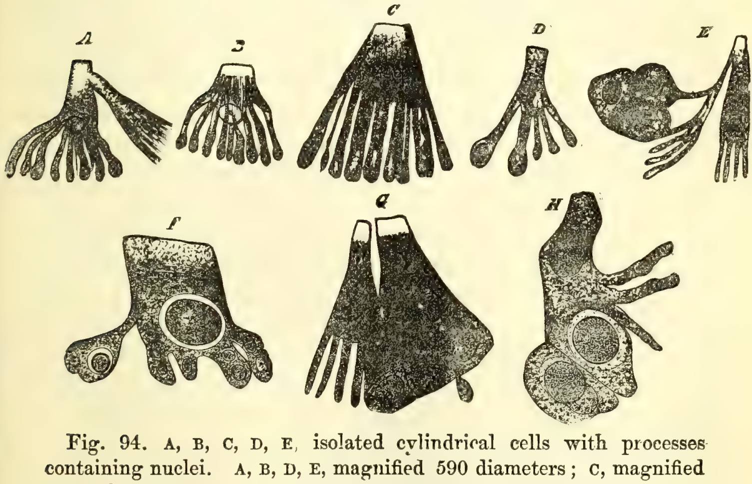

Fig. 94. A, B, C, D, E, isolated cylindrical cells with processes containing nuclei. A, B, D, E, magnified 590 diameters; C, magnified 1,200 diameters. F, G, H, cylindrical cells with processes, which are evidently young cells, and form at G a beautiful mosaic. Magnified 1,100 diameters.

breaks up into several filaments, so that groups of branched processes appear to have budded forth from the columnar cells, which often form thick brushes, the base of which is formed by the small columnar cell. In the next place, the free extremity of these fibres is enlarged into a kind of head, resembling a small club, that forms a minute corpuscle (fig. 94). These clavate extremities may be seen to increase in size till they are clearly distinguishable as cell nuclei, surrounded by a sparing quantity of protoplasm. This process of formation of nuclei commences from infinitesimally small points in the fibre, and extends towards the columnar cells, so that two, three, or even very many may originate in one fibre. The small clavate extremities gradually enlarge to form salivary cells, and after a time it is not difficult to find such epithelial cells constituting the mosaic-work of the alveoli, and directly continuous with the columnar cells by means of processes (fig. 94, E). Usually the processes are of such a form that the fibres of the brush attached to the columnar cell increase in size as they recede from it, and develop a very delicate protoplasm, in which larger or smaller nuclei are contained.

Since it always occurs that a large section of a salivary tube is implicated in this remarkable process of cell formation, and since the most active growth takes place upon the membrana propria, the wall will be found to be enormously thickened and laminated, with primary and secondary projections, whilst the young cells enlarge and arrange themselves in the form of a mosaic. But coincidently the connective tissue projects inwardly into the thick wall, separating off the cells into alveolar-like groups. I have observed this process of the projection of alveoli *en masse,* as it were, from the salivary tubes of a columnar cell, particularly well in the sublingual gland of the rabbit. The degree of ripeness which the various cells contained in one alveolus exhibit is not always the same; thus it is customary to meet with a few young cells at the periphery of the alveoli in mucous glands (such as the submaxillary of the dog, ox, and rabbit). How is this process of new formation of salivary cells to be explained? They are formed in the processes of the columnar cells, without the nucleus being in any way implicated; for, even when these

processes contain numerous nuclei, the nucleus of the columnar cell still appears to be always perfect, spherical, sharply defined, and without a trace of gemmation. Even with the highest magnifying powers I have never observed any indication that a filament was given off from the nucleus which could serve as a point of origin for the young nuclei. A few processes even pass over the nucleus through the columnar cell,

Fig. 95.

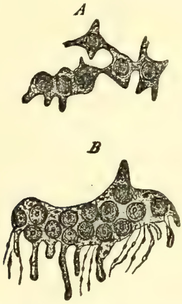

Fig. 95. Multiplication of nuclei in the dilated and swollen processes of the columnar cells. A, formation of small multipolar cells; B appears to be a dilated process of a columnar cell. Magnified 590 diameters.

and their striæ run parallel to its axis as far as to the free surface directed towards the cavity of the salivary tube, so that it scarcely appears to be possible that the nucleus originating in the extremity of such a process could be derived from the nucleus of the cylinder cell. The latter is almost always single, rarely double. Very small and non-nucleated columnar cells, possessing processes that are filled with small nuclei, are also sometimes present (fig. 93). As on this ground I do not feel myself justified in attributing the origin of the new nuclei developing in the processes to that of the columnar cells, we must admit that we have before us a case of free cell formation, if under this term we understand that mode of cell increase in which the newly developed nucleus originates independently in a cell, and is not a morphological element proceeding from a division of a previously existing nucleus. When we see the axis cylinder and its fibrils to be directly continuous with the fibrils of the

columnar cells, without any difference being perceptible between the axis cylinder and the fibrils of these cells, we may legitimately describe the nerve as extending to the point where it joins the substance of the body of the cell. That is the most natural explanation that can be given. This explanation, however, possesses the greatest significance in regard to the mode of development of the glandular epithelium, because it directly follows that the young nuclei originate in the axis cylinders, and that the gland cells which at a later period seem to constitute a thickening of the axis cylinder bud forth, as it were, from the nerves. This explanation renders it intelligible why the nucleus of the columnar cells are so indifferent during the multiplication of the epithelium. In opposition to this view, which I regard as the most probable, it may be urged that, in consequence of the intimate fusion of nerve substance and epithelium at the periphery, no sharp limit can be drawn, showing where the one ceases and the other begins; and that, moreover, it is probable that imperceptibly fine processes are given off by the nucleus of the columnar epithelial cells, which become detached at an early period by fission. That the nuclei of the salivary cells have processes, cannot, however, be regarded as forming a valid objection to my view, since the young nuclei may really be thickenings of the axis-cylinder fibrils.

I may further adduce, as a weighty argument in favour of my view, that the fibrils of the axis cylinder do not terminate at the surface of the fully developed salivary cells, but, as in the case of the ganglion cells, may be traced into their very substance.

Now, since the finest axis cylinders and fibrils extend to the columnar epithelial cells, and are connected with the processes that are in course of development, and since portions of these processes subsequently become large salivary cells, connected with thick medullated nerve fibres, it follows that the nerves must increase coincidently with the young epithelium to which they belong. Amongst these metamorphoses there also occurs a mode of termination of the medullated nerves, to which I some time ago called attention, and which consists in the nerve suddenly undergoing frequent division, then enlarging, and containing finely granular protoplasm, with many nuclei of

various sizes. I have named this mode of nerve termination, that by a "protoplasmic foot." If, as I have sometimes observed, many of the nuclei appear to be provided with fibres, which can be followed into the interior of the nerve fibres, it is highly suggestive of the development of the gland cells from the nerves.

In regard to every explanation it must be observed that transitional forms may occur, respecting which it is impossible to say whether they are epithelial or nervous. The continuous and luxuriant neoplastic formation taking place in the substance of the salivary ducts presupposes their regeneration, respecting which I have formed my own opinion, but have arrived at no definite conclusion. In like manner the persistent neoplastic formation of the alveoli in adult animals determines an atrophic detachment of those already present. In Moles I have sometimes found the alveoli with pale offshoots of various forms, and pale finely granular contents, which may be such atrophied and separated alveolar segments.

I first comprehended the complexity of all forms of salivary glands when I recognised the constant production and disintegration taking place in them, which is referrible to the nerve substance.

§ 6. The Morphological Constituents of the Saliva.—Healthy saliva contains no morphological elements, but forms a transparent perfectly homogeneous fluid. But when the mucous membrane is irritated, either by ligature of the excretory duct, or by the introduction of a canula into its interior, we obtain isolated morphological elements, which are continuously developed by a kind of catarrhal condition and exudation. The appearance of these has led some observers to the belief that normal saliva contains formed elements, and continually carries off glandular epithelium. As recent investigations have been in direct contradiction to these statements, I may perhaps be allowed briefly to state the grounds on which my opinions are based. When, in a dog, the duct of Wharton and the nerves supplying the submaxillary gland have been exposed, isolated, and divided, a watery saliva flows from the duct, as transparent as a dewdrop. The secretion found in the

duct is also clear. If a canula be now introduced, and firmly tied in, and the nerves be irritated, the fluid immediately becomes cloudy; but when a few drops have been discharged, it again resumes its transparency. The first drops discharged on irritating the nerves, after the introduction of the canula, are those which were already in the duct, and were originally transparent, but have become cloudy whilst still in its interior, for the clear secretion extracted from the freshly excised duct remains clear when exposed to the air. Contact with the wall of the duct has consequently rendered the secretion cloudy. If we examine the first drops microscopically, we shall find they contain isolated cells and groups of epithelial cells with nuclei, unquestionable medullated nerve fibres, connective tissue, etc.; in a word, constituents which have been detached from the mucous membrane of the duct by the canula, and which there is no object in describing further. As soon as a stronger salivary current is induced by excitation of the chorda tympani, these detached elements are completely washed away, the fluid again becomes quite clear, and no longer contains any morphological elements. After a short time, however, they reappear in sparing number as the so-called salivary corpuscles, that is to say, as small, finely granular, nucleated cells, presenting in some instances amœboid movements, whilst the fluid is rendered cloudy by the presence of fine granules. These bodies, however, it may be easily shown, always proceed from the wall of the excretory duct after it has become affected with catarrhal inflammation, and not from the gland; for if the nerves are irritated sufficiently long to cause a flow of perfectly clear saliva from the india-rubber tube of the canula, and the excitation be then interrupted for ten minutes, and, before it is recommenced, the saliva stagnating in the caoutchouc tube from the previous irritation be pressed out, it will be found, when collected, to be as clear as before. If the excitation be now reapplied, we obtain, since the canula is of very small diameter, for the first three or four drops, that which has collected in the excretory ducts from the previous irritation. These three drops are quite cloudy from exudation and detached cells, but are followed immediately by saliva as clear as water; that is to say, as soon as the exudation has been washed out of the duct. I

have estimated the capacity of the duct from the canula to the gland, and am of opinion that it will contain about three drops. The quantity is certainly very much smaller than the total secretion which, in the period before the renewed excitation, stagnated in the very numerous and, in some instances, very wide ducts. Thus it appears that the originally clear saliva contained in the duct has become cloudy, and obviously in consequence of a pathological process; for, if a freshly exposed duct be emptied of its contents, even if the dog have previously discharged no saliva, the secretion obtained on section is clear.

The saliva caused to flow by irritation of the sympathetic nerve contains a large number of spheroidal particles of mucus, together with morphological elements of a less clearly definable nature, but representing products of disintegration. Heidenhain, however, was frequently unable to discover any morphological elements. As this kind of saliva can only be obtained in small quantity, the exudate that is poured forth may perhaps never be completely washed out and evacuated, and as only a small quantity of saliva appears at long intervals, the fluid essentially consists of this. Heidenhain has shown that when the excitation is long maintained it becomes clearer. The relations of the sympathetic nerve to the salivary glands are, however, involved in much obscurity.

From what has now been adduced, it will be seen that further observations are required before it can be admitted that the saliva naturally contains formed elements.

§ 7. Of the Alteration of Structure in the Glands caused by the Performance of their Functions.—When the salivary glands have been long in action, they become lighter, softer, paler in appearance, and both absolutely and relatively poorer in solid constituents. After being long at rest the inverse changes occur, and they assume a yellower colour. This last I believe to be occasioned by the accumulation of numerous molecules in the salivary cells. The gland becomes "charged." Heidenhain has recently expressed the opinion, that in some animals (Carnivora and Herbivora) the secretion is accompanied by the disintegration of a certain proportion of salivary cells, the place of which is supplied by a new genera-

tion developed at the periphery of the alveoli. In rabbits, the secretion of saliva in the submaxillary gland is effected, according to Heidenhain, exceptionally without demonstrable *disintegration and neoplastic cell formation.*

The important and novel principle in respect to the action of the nerves, established by the observer just mentioned, cannot be here passed over in silence. I have placed an investigation into the accuracy of his statements into the hands of my pupil, Herr Anton Ewald, of Berlin, who has been for some time engaged under my superintendence with the structural changes induced by excitation of these glands, and has pursued precisely the same method as that adopted by Heidenhain. After one submaxillary gland had been excited for a considerable period (as long as for seven hours) whilst the other had been kept at perfect rest, both were removed from the living animal, and from these thin sections were made with a razor, which were immediately thrown into a large quantity of absolute alcohol. By this means we avoided, as far as possible, in the unexcited gland, which is charged with mucus-forming substance ("mucigen"), the production of any material structural alteration through the *post-mortem* formation of mucous vesicles in the alveoli, consequent upon displacement of cells and protoplasm. This precautionary measure was not unnecessary; for in the gland, which has been for a long time actively discharging its function, no more "mucigen" is contained, and, therefore, in this case, no alteration of structure can occur from the formation after death of mucous vesicles.

When both glands had been hardened for an equal time in alcohol, very fine sections were prepared, macerated for the same period in the solution of carmine in glycerine, employed by Heidenhain, and finally, after the most careful washing, examined in glycerine. It is obviously a matter of great importance that the sections should be made as fine as possible, and all those that are thicker than the diameter of a salivary cell should be rejected. If the cell mosaic lining the interior of the alveoli of the quiescent gland be examined, we find for the most part a single layer of *sharply defined transparent* polygonal cells flattened by mutual pressure, which, however, are not perfectly hyaline, but exhibit a delicate *striation,* as though

a perfectly transparent substance were traversed by numerous extremely fine pale fibrils. These salivary cells, which, on account of their contents consisting in the Dog chiefly of mucus, with but little albumen, Heidenhain has termed "mucous cells," are more or less, though in general but slightly, tinted with carmine. When the staining is more strongly marked, the cells contain albumen. A structure, which is probably the nucleus of the mucous cell, lies together with a little protoplasm at the periphery of the alveolus, and resembles the process of the cell in being stained of a deep red colour. Inasmuch as all the processes, together with the nuclei and protoplasm, are situated at the periphery of the alveolus, a broad red zone is here frequently formed. Here and there one or more salivary cells appear more or less deeply tinged with carmine. These cells are named by Heidenhain the "crescent." He regards them as the earlier stages of development of the cells which gradually become "mucous cells," which, I think, is not improbable. He silently acquiesces in the view I have stated above, that all salivary cells do not behave in the same manner with reagents, a difference that I am disposed to attribute to their various grades of development.

If we now consider the excited gland, the differences which present themselves are, that *all the cells are stained with carmine,* though perhaps only slightly, some being more strongly tinted than others—the staining, however, independently of the protoplasm, being, on the whole, less marked than in the quiescent gland; that no evidences of *multiplication by fission* of the young cells at the periphery of the alveoli are visible, in corroboration of which I may refer to Plate i., figs. 84 and 85 of Heidenhain's Essay; that *all the contour lines* are remarkably pale and softened off, especially those separating the alveoli and the salivary cells, which are *no longer defined by thick lines;* that the nucleus is *less* reddened, *more delicately* contoured, *larger,* and, generally speaking, *spheroidal.* The effects of the excitation consequently are, that instead of cells *not becoming stained with carmine,* with round nuclei *shrinking* in alcohol, and becoming intensely stained with carmine, we obtain cells *reddening* with carmine, containing nuclei which undergo *no shrivelling* in alcohol, and are less deeply stained with carmine.

Heidenhain draws the conclusion from these facts, that the first form are disintegrated in the act of secretion, whilst the second are newly developed.

There still remains the possibility that the "mucous cells," in consequence of their persistent activity, have undergone an essential alteration in their chemical constitution, to which the differences in their appearance are attributable, according to whether they have been at rest or long in action. I cannot, however, deny that the completely different appearances (see fig. 95) presented, strongly support Heidenhain's opinion.

Heidenhain lastly adduces, in support of his opinion, the circumstance that he was able to isolate a larger number of cells undergoing fission from the excited gland, after maceration in iodized serum, than in that which has been kept at rest. The epithelial cells of the salivary glands of the dog are generally isolated with difficulty. The isolation of the younger cells in the excited gland may perhaps be facilitated by this very excitation rendering them looser, softer, and more watery, as Heidenhain himself remarks. May not also the continuous streaming of saliva, rich in the corroding carbonate of soda, favour their isolation? It is further noticeable that, according to Heidenhain, these young cells, after long maceration, become isolated sooner than other kinds of epithelia, showing that, under favourable circumstances, they are formed earlier or in larger numbers. I must further observe, that, in accordance with my experience, I can demonstrate in every quiescent salivary gland thousands of epithelial cells in the act of multiplication. The sublingual gland of the rabbit is particularly well adapted for this purpose, offering the additional advantage that, like the submaxillary gland of the dog, it exhibits large and beautiful mucous cells and semi-lunar bodies. In any such gland, thousands of young epithelial cells, developing by the process of gemmation, may be discovered. I hold a gradual process of disintegration of the alveoli to be highly probable, on the ground of that regeneration of salivary cells which I discovered to proceed from the cylinder cells of the excretory ducts. The question as to how far the nervous system exerts a primary or a secondary influence on this vegetative process still demands further investigation.

Fig. 96 A.

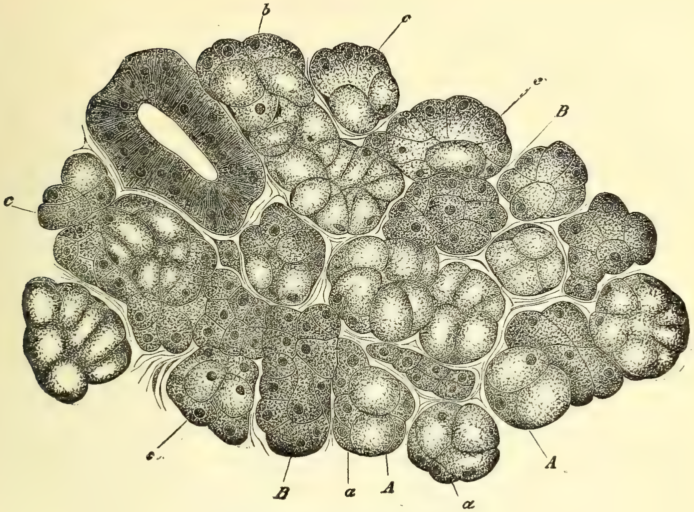

Fig. 96 A. Quiescent gland.

Fig 96 B.

Fig. 96 B. Exhausted gland from the Dog, after Heidenhain.

K. K.

§ 8. THE STROMA OF THE SALIVARY GLAND.—The connective tissue consists partly of membranes, partly of fasciculi of fibres, which form a porous network traversing the whole organ, and are commingled with a larger or smaller number of elastic fibres, that are often developed to a very large extent. The nuclear structures are not in general readily demonstrable, but when present, appear as small oval, sharply defined, highly refractile corpuscles. In some places, finely granular nucleated cells are found, with thick processes, which must, in all probability, be also regarded as amongst the cellular elements of the connective tissues. As we have already mentioned, pale, flattened connective tissue cells form, according to Boll and Kölliker, a reticulum around the alveoli.

In regard to the presence of the muscular fibres that Schlüter states he has seen in the stroma, I beg to observe that I have recently directed my especial attention to the determination of this point, which on physiological grounds is of great importance; and that in sections of the gland which had been stained with carmine, hardened in alcohol, and examined in glycerine, I have been able to satisfy myself of the presence of, in some instances solitary, in others of fasciculi of smooth, fusiform muscular fibre cells, with elongated rod-like nuclei, that certainly could not be regarded as constituents of the vessels, and must confer some, though perhaps only slight, contractility on the stroma.

The connective tissue stroma intervening between the alveoli attached to a single excretory duct is exceedingly small in quantity, so that the alveoli lie closely compressed and flattened against one another. The several grape-like masses of glandular substance belonging to different small excretory ducts are separated from one another by broader bands of connective tissue, in which, when the animals are fat, fat cells are seen, resulting from the conversion of connective tissue cells, so that treatment with perosmic acid brings into view a delicate marbling, formed of black lines, in every fresh section of a gland. Where the secondary and tertiary groups of grape-like glands belonging to a larger excretory duct are united into a compact mass, numerous lobules are formed, visible with the naked eye, and divided from one another by fissures. The walls of these

fissures are composed of connective tissue fibres, and I have observed them to be lined by an indistinct endothelium. Nevertheless, I have, up to the present time, found no functional peculiarity connected with these structural features. I do not in the least doubt that the fissures belong to the lymphatic system, as Gianuzzi maintains. Nothing definite is known in regard to the anatomy of the bloodvessels, which stand in such a remarkable relation of dependency to the nervous system, nor yet in regard to the lymphatic vessels. The capillaries wind around them in close contact to the membrana propria forming a very close plexus, derived from different quarters, and show no points of difference from the ordinary arrangement.

§ 9. Mode of Investigation.—If it be desired to obtain a general view of the arrangement of the alveoli, excretory ducts, cells, and stroma, fine sections should be made of hardened glands. The hardening is best effected by placing thin portions, whilst still warm from the body, in absolute alcohol. Fine sections can then be made, tinted as usual with carmine, and examined in glycerine. In order to study the finer structural relations, every method of hardening must be avoided. Sections made with very sharp knives of the perfectly fresh gland, can be examined in iodized serum, or in chromic acid containing from 25 to 50 per cent., to which a little iodized serum has been added. When thin sections, thus made, are carefully broken up with needles, isolated alveoli may be obtained, with salivary tubes, epithelial cells with nerve terminations, and the like. The isolation of the epithelial cells is best effectedby the application of iodized serum, in which the gland has been allowed to macerate for from four to six days, or still better, by treatment with iodized serum, subsequent to maceration in chromic acid of one half per cent. The chromic acid macerates the glands most advantageously, if one or two glands have previously been lying in it for one or two days. When quite freshly applied, the volume of this reagent should not exceed from two to four times the volume of that of the gland. Another method of isolating the elementary constituents, especially of the glands in the rabbit, consists in placing the latter in a small test tube, and adding from four to eight drops of solution of chromic acid,

containing one-fiftieth per cent. After the course of an hour, when the organ appears hardened and translucent by imbibition, fine sections may be prepared and broken up by fine needles in the same solution. Solution of caustic alkali, containing 33 per cent., is also well adapted for the isolation of the elementary parts. As soon as the gland has become brown, which occurs in a quarter or half an hour, the tissue can be easily broken up. The liquid in which the preparation is examined, it is obvious, must not be water, but always the same solution of alkali. A method especially adapted for the demonstration of the mode of nerve termination is that introduced by Max Schultze, which consists in laying the fresh gland in perosmic acid, and thus staining the medullated nerves of a dense black colour, causing them to resemble tubes injected with ink, whilst the epithelial cells, examined in thin layers, are scarcely, if at all, coloured. The salivary tubes only assume a brownish tint.

CHAPTER XV.

STRUCTURE AND DEVELOPMENT OF THE TEETH.

By W. WALDEYER.

HARDENED structures of the animal organism, similar to those which are called teeth, though certainly presenting very various histological structure, are found widely distributed both amongst the vertebrate and the invertebrate series.

With the exception of the larval form of Petromyzon (Ammocœtes); of Amphioxus, Accipenser, and the Lophobranchii (Cuvier), amongst Fishes; of some Toads (Pipa), amongst Amphibia; of the Chelonia, amongst Reptiles; of the entire class of Birds; and of the Myrmecophaga, Manis, and Echidna, amongst the Mammals, all vertebrate animals possess teeth. In the whale-bone Whale they are present in the fœtal state.

The anatomical model of a tooth of a vertebrate animal is a large papilla of the mouth or of the pharyngeal mucous membrane, which, in consequence of chemical and histological conversion of its constituents, has acquired a remarkable degree of hardness. And, according to whether the connective tissue substance of the papilla participates in the hardening or not, two large groups of teeth are distinguished—dentinal teeth and horny teeth.

The horny teeth are by far the most simple in their structure. They appear as more or less developed papillæ covered with a thick horny investment. They are never continuous with portions of the skeleton, but constitute the transition to other horny formations, as hairs, stings, etc. True horny teeth are met with in the Petromyzidæ, the Myxinoids, and in Ornithorhyncus. The whalebone of many whales, and the horny masticating plates of Rhytina Stelleri, though remark-

ably complex structures, yet clearly belong to the same series of formations.

Fig. 97.

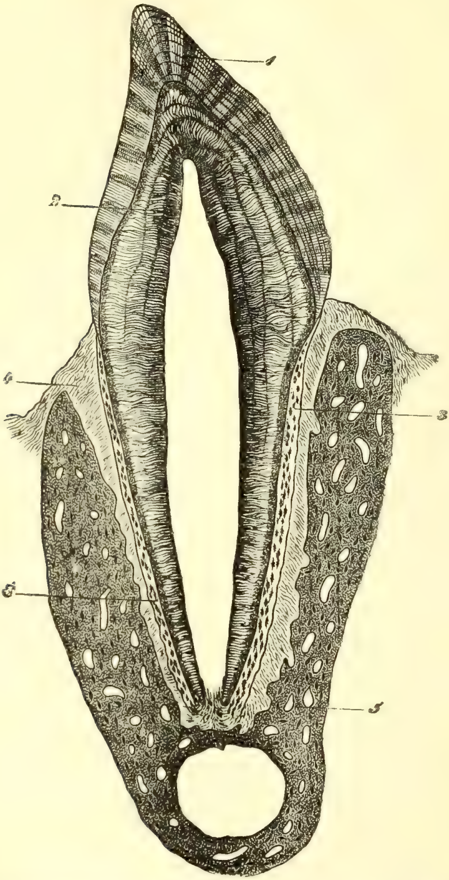

Fig. 97. Premolar tooth of the Cat, *in situ*. Vertical section, magnified 15 diameters. 1. Enamel with decussating and parallel striæ. 2. Dentine with Schreger's lines. 3. Cement. 4. Periosteum of the alveolus. 5. Inferior maxillary bone.

In the dentinal teeth the connective tissue matrix of the papilla plays a most important part in the hardening process, which here proceeds in a manner precisely similar to the ossify-

ing process, except that no true bone is formed, but only an allied substance of much harder consistence, and differing more or less in histological structure, termed *dentine.* The epithelium of the tooth papilla either atrophies to a rudimentary horny investment, the *cuticula* (membrane of the enamel), or it becomes elongated in a remarkable manner into long petrified prisms, which collectively invest the dentine, and are known as the *enamel.* In addition to these there is found an accessory structure, the *cement,* a true bony substance, which especially invests the fangs of the teeth. Dentinal teeth are constantly attached to the parts of the skeleton surrounding the mouth and pharynx, and for the most part to the lower jaw.

From the simple arrangement of the three chief constituents of the teeth, as they occur in man, for example, there are manifold and complex variations. Amongst these may be enumerated in particular the so-called folded enamel teeth of Rodentia, Solipedes, and others, and the compound teeth of many fishes and fossil reptiles (Labyrinthodon), of the elephant, etc. The "folded enamel" teeth, dentes complicati, are formed on the type of a simple tooth. The dentine of the crown is, however, folded like a ruff, and the enamel and cement dip in to form a covering to the surface of all the sinuosities. Of the dentes compositi two principal forms can be distinguished. In one, a common stem or trunk is present, which gives off a number of separate toothlets (Galeopithecus, Labyrinthodon), whilst in the second a common tooth pulp is absent, and instead we find, as in many fishes and Orycteropus, numerous independent toothlets proceeding from the jaw, and united to form a common tooth. The pulp of the teeth of the Labyrinthodonts is therefore comparable to the compound filiform papillæ of the tongue ; whilst the true compound teeth of the second class bear the same relation to simple teeth that the hoof does to hair. The several back teeth of the Elephant have the characters of the first kind ; each separate tooth, however, presents folding of the enamel, so that a highly complex structure results.

On the other hand, the structure of a tooth may be simplified by the absence of one or two of the above-mentioned dentinal tissues, especially the enamel, or the enamel and cement. Thus the tusks of the Elephant and the teeth of the Edentata have no enamel ; and again, in the case of the Rodents, the masticating surface of their incisor teeth has no enamel. According to Owen (34), the pharyngeal teeth of Labrus are composed of ordinary dentine alone. Amongst

Fishes, as, for example, in the Pike, a common arrangement is the combination of a central mass of vascular dentine (vaso-dentine, Owen), with a thin cap of ordinary dentine, which in the most external layers is homogeneous, and very hard (vitro-dentine, Owen, 34). Compare fig. 99.

Dentine (Substantia Eburnea, Ebur).—Dentine forms a yellowish-white, highly elastic, but friable mass, presenting a finely fibrous, peculiarly lustrous fracture, and is one of the hardest constituents of the animal body. Its chief components are a very firm matrix, analogous to compact bony tissue, and extremely fine, frequently branched fibres—the *dentinal fibres* of Tomes (40) and Kolliker (58), which occupy fine canals, the *dentinal canals* traversing the matrix. The dentinal fibres are enormously elongated processes of the the so-called dentinal cells, or cells of the dentinal pulp *(odontoblasts)*. Dentine consequently corresponds to bone, with this difference, that instead of cells it contains the long processes of cells in its calcified matrix. In regard to the other characters of the matrix, it presents a similar uniformity of appearance, and a similar chemical composition, to that of compact bone. After treatment with acids (especially with dilute hydrochloric acid) a material, *dentinal cartilage*, is obtained which is precisely similar to ossein, except that it is of somewhat firmer consistence.

The dentinal fibres constitute the soft parts of dentine. They do not lie in direct contact with the hard matrix, but are invested by sheaths, the *dentinal sheaths* of E. Neumann (48), which are intimately connected with the matrix. After the fibres have been removed by maceration, or by incineration of the tooth, the dentinal sheaths remain, and even after destruction of the matrix by boiling in strong muriatic acid or in caustic alkalies, they constitute the only perfectly indestructible residue of the tooth. They form the white finely fibrous felt which still remains after treatment with the above-mentioned reagents. The dentinal sheaths, it is highly probable, belong to the category of elastic limiting layers which not unfrequently form around the cavities of the connective tissues. E. Neumann considers them to be calcified (see also p. 125).

The dentinal matrix, then, is traversed by a number of fine

canals, having walls of a peculiar nature—the dentinal sheaths —in which lie the dentinal fibres. The *dentinal canals* commence with small circular openings on the inner surface of the pulp cavity, and pass radially outwards through the dentine, making numerous spiral turns in their course (Welcker, 41).

Fig. 98.

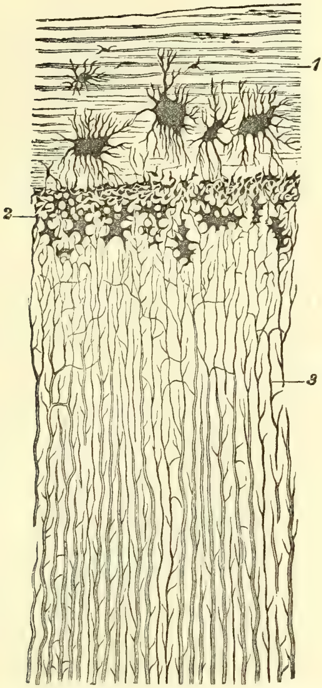

Fig. 98. Canine tooth of Man, presenting a portion of the transverse section of the root. 1. Cement with large lacunæ and parallel striæ. 2. Interglobular substance. 3. Dentinal tubules. Magnified 300 diameters.

As a general rule each tubule extends from the pulp cavity to the enamel, or cement, giving off in its course numerous delicate transverse branches. By means of these transverse branches both the tubules and their contents—the dentinal fibres—anastomose with each other. In sections made from

fresh teeth, examined with high powers (500—1,000), it is not difficult to recognise, especially in the central section of the course of the tubules, which is of considerably larger diameter, the pale homogeneous dentinal fibre. The lining of the tubules (dentinal sheaths) can only be satisfactorily seen in cross section, when they appear as delicate yellowish rings, in the interior of which the transverse section of the dentinal fibre is perceptible in the form of a minute dark point. I, at least, agree with Kölliker (58) in this interpretation of the appearances seen on cross section. Carious teeth prove very serviceable in exhibiting these relations.* The dentinal tubules are best examined in fine sections dried in air. They then make their appearance, filled with air, in the form of strongly defined very dark tubules or lines, enabling them to be traced to their finest ramifications.

In regard to the mode of peripheric termination of the dentinal tubuli no positive conclusion can be drawn. Yet exact information on this point is of considerable importance, because Tomes (29) has directed attention to the sensibility of the peripheric portion of the dentine.

Wherever the terminal loops occur the dentinal tubuli must also end in the same manner; nevertheless, it is difficult to demonstrate actual terminal loop-like structures. Extremely fine processes of the dentinal tubuli run towards the enamel, and are lost at the surface of the dentine. At this part also larger or smaller irregularly defined cavities are found, *the interglobular spaces* of Czermak (33), which will be more fully considered hereafter. The dentinal tubuli open into these interglobular spaces, and from them again fine processes extend towards the enamel. A direct passage of the dentinal tubuli into the enamel does not occur.

Tomes (29) and Kölliker (58) are strongly of opinion that some of the dentinal tubuli, with their soft contents, penetrate into the enamel. This they think especially occurs amongst the Rodents and Marsupials. I have not, however, been more successful than Hertz (52) in con-

* In the vicinity of carious portions of tooth, both the soft dentinal fibres and the dentinal sheaths are thickened, so that in transverse sections both come very clearly into view.

vincing myself of this fact. No conclusion can be drawn with positive certainty from sections, since the slightest deviation from parallelism in the surfaces may easily produce deceptive appearances. So, again, fissures in the enamel, and inequalities of the adjacent surfaces of the dentine and enamel, might easily lead to the view supported by Tomes. The question can only be determined by the examination of young teeth in process of development; but I have never been able to discover anything of the kind. Intervening between the dentine and the cement is a considerable quantity of the already mentioned interglobular substance, and the greater number of the dentinal tubuli open into its irregular spaces. These again are continuous with the lacunæ of the cement by means of fine canaliculi. The tubuli may be followed quite to the free surface of the masticatory surface of the incisor teeth of the Rodents, where the dentine is freely exposed; but it appears to me that in the peripheral portions of these tubules the dentinal fibres are atrophied.

If we now proceed to consider the *dentinal fibres* with more minuteness, no further reference to their course and direction is needed, since these are determined by that of the tubules, which have already been sufficiently described. At the same time it is not easy to decide whether the fibres are present in the finest peripheric ramifications of the tubules. In young teeth this is certainly the case, but in those that are older atrophy of the fibres appears to be concurrent with obliteration of the canaliculi. We may seek in vain, even in young dentinal fibres, for rudiments of nuclei, although both the history of their development and several pathological appearances (as for instance those accompanying caries) might lead us to expect their presence. The fibres easily stain with carmine. They possess a remarkable degree of extensibility, so that, especially in young teeth, the dentinal cells may be separated to a considerable distance from the dentine without rupture of the processes, which then appear like harp strings stretched across the interval. Salter (51), in recently describing the fibres as tubules, because, when dry, they appear to contain air vesicles, and exhibit a dark central point on section, has probably had the dentinal sheaths under observation. The fibres are really completely solid and homogeneous.

There are some remarkable deviations from the above-described

structure of the dentine. The *interglobular substance* is in the first place a structure tolerably widely distributed. Czermak has described under this name those parts of the dentine which, when thin sections are dried in air, appear beset with irregular spaces and cavities. The walls of these spaces, especially if they form a deep notch, often project in the form of spheroidal masses or dentinal globules. Indications of a spherical form which sometimes occur in the compact dentine are explicable on the supposition that the interglobular spaces have been obliterated by calcification of their soft contents, the contours of their original walls being to some extent retained. The contents of the interglobular spaces consist of a soft mass. In the young fresh teeth of the calf, rounded and stellate cells may frequently be seen in the larger interglobular spaces, with processes which extend into the dentinal canals opening into them. At a later period the cells atrophy, or their protoplasm becomes converted into a substance analogous to the dentinal cartilage. In immediate proximity to the cement, a layer of very small, closely compressed interglobular spaces is very constantly present, forming the *granular layer* of Tomes. The interglobular spaces, with their soft contents, are therefore only the result of a somewhat irregular process of dentinification, and are analogous to the small irregular medullary cavities found in the interior of compact bone.

In the dentine of many animals, especially of Fishes, of some Rodents, in the central portion of the tusks of the Elephant, the molar teeth of the Iguanodon and others, vascular canals exist analogous to the Haversian canals of bone, constituting the *vaso-dentine* of Owen. In Man this form of dentine is only met with as a consequence of the secondary ossification of the pulp. In many Fishes (Kölliker, 45) the bones of the skeleton consist in great part of true dentine; whilst conversely we find in the dentine of the teeth, especially in pathological conditions, masses with bone lacunæ, termed Odontomes by Virchow, and Osteo-odontomes by Hohl, which occur in the dentine near the cement, or in ossifications of the pulp, and form the *osteo-dentine* of Owen.

Transitional forms, between vaso-dentine, osteo-dentine, and ordinary dentine, are frequently met with in Fishes, as, for instance, in the Pike. In the Cetacea, Dugong, and Physeter, again, the peripheric layer of the dentine, which contains a large number of small interglobular spaces and true bone corpuscles, passes without interruption into the investing cement, so that it is impossible to draw here any definite line between osseous substance and dentine.

Schreger (7) first recognised a system of concentric lines running

parallel to the contour of the teeth in dentine, which in large teeth can be easily seen with the naked eye, or with a low magnifying power. In true dentine they present on section a characteristically decussating course with small rhomboidal meshes between them. As Retzius (19) and Owen (25) first correctly stated, the lines of Schreger are occa-

Fig. 99.

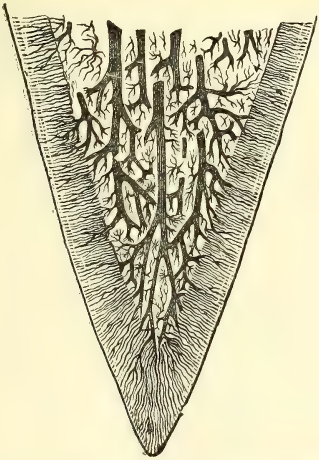

Fig. 99. Apex of a tooth from the lower jaw of the Pike (Esox lucius). Magnified 80 diameters. The central portion consists of vaso-dentine, which is covered with true dentine; external to which again is a thin layer of vitro-dentine.

sioned by the corresponding primary curvatures of the dentinal tubes. Owen (25) describes in addition a second system of parallel curved lines in dentine, the *contour lines* occurring especially in the tusks of the elephant, produced by regularly intercalated strata of small cells (probably finely granular interglobular substance). Czermak and Kölliker give similar illustrations, drawn from the teeth of man; we are not however justified from these appearances in concluding that dentine possesses a lamellated structure.

Enamel (Substantia Vitrea; Subst. Adamantina; Encaustum; Adamas; Email).—Enamel is the hardest substance met with in the Vertebrata, being in this respect about equal to Apatite (F. Hoppe-Seyler, 69). With its translucent mass and bluish tint it forms a kind of cap of various thickness, investing the

crown of the tooth, usually following its contours with accuracy. Its surface, especially at the sides, exhibits very fine, nearly parallel, transverse striæ (Czermak), which are probably referrible to the papillary structure of the *enamel organ* (see this). Coarser projections with deep grooves, which have likewise been described by Czermak, must be regarded as pathological formations.

In young teeth, examined at that stage in which the enamel is still soft and capable of being cut with a knife, it is easy to demonstrate that it consists of rather elongated prisms of about 3—5 μ long, which are called *enamel fibres, or enamel prisms* (see fig. 103, 4 and 5). It is impossible to avoid perceiving a certain similarity in form between these and very long columnar epithelial cells, like those which form the fibres of the lens. This is especially obvious in fine transverse sections, which exhibit a delicate mosaic with six-sided areas. After cautious treatment with dilute hydrochloric acid and subsequent boiling in $S\,O_3$ (Beigel (50), whose method otherwise affords no special advantage), the enamel prisms can be easily isolated in adults. Their extremities are often pointed like a needle, which, however, appears to depend only on irregular fracture. By the same means, also, it can be shown that the prisms partly run in a straight direction, and partly in curves; but I have not been able to satisfy myself that angular or zigzag curvatures occur, as stated by Czermak. The dark transverse striæ and slight varicosities which, especially after the addition of very dilute hydrochloric acid, occur at regular distances from one another in the isolated prisms of enamel, are very remarkable. If the treatment with hydrochloric acid be continued for some time longer, the fibres split in the direction of the clear transverse lines into small cubic fragments of nearly equal size (3—4 μ).

It still remains a question how the transverse bands are to be explained. The circumstance that they are generally absent, or at least are not so well marked in young soft fibres, and that their relative thickness nearly corresponds to the thickness of the fibres, has led me (49) to express the opinion that they might proceed from the decussation of the fibres. I am well aware of the grounds adduced by Hertz (52) against this supposition, and which are assented to by

Kölliker; but I must still consider it doubtful whether all enamel prisms exhibit transverse striæ and varicosities. Hertz returns to the intermittent (schubweise) calcification of the enamel cells formerly admitted by Hannover (39). But the mode in which so regular a transverse striation is thus produced, is, to me at least, unintelligible; besides, no evidence can be brought forward showing that a laminated mode of formation occurs in enamel.

The enamel fibres lie in close contact with each other, without any demonstrable intervening substance. They appear to be completely solid, and extend for the most part through the whole thickness of the enamel. At the same time they pursue a very various course, which finds its expression in the well-known *decussation* of the prisms. We accordingly find that alternate layers of enamel fibres appear on section to run vertically and transversely, in consequence of which a peculiar and sometimes very regular pattern is produced. The enamel prisms must therefore also pursue, in the form of fasciculi, a various and often decussating course towards the surface of the tooth. A second pattern presenting itself in the enamel is formed by the so-called *brown parallel striæ* of Retzius, which are superimposed lines coursing in the same direction, and regarded by Kölliker as the expression of a laminated mode of formation of the enamel.

These are frequently (see fig. 97) very fine, and closely applied to one another; some appearing to be more conspicuous than others. No satisfactory explanation of this phenomenon can at present be given. Hertz attributes it to deposits of pigment in the enamel prisms, as occurs, for example, in the beaver and squirrel, where it is due, according to V. Bibra (68), to the presence of oxide of iron; and in these Rodents, according to Wenzel (66), such deposits are already present in the protoplasm of the enamel cells; still, no positive statements can at present be made on this point. Other kinds of striæ, again, may be perceived on examining transverse sections, and most distinctly after brushing with dilute hydrochloric acid (1 : 12, Hertz), which are caused, according to Czermak, by the regular zigzag course, or, according to Hannover, by twisting or spiral turns of the prisms. An explanation will be hereafter given of the decussation of the prisms, as well as of their various course (see the Development of the Enamel). The observations of Hoppe-Seyler (69) on the behaviour of the enamel

in polarised light are replete with interest. According to these, fully developed enamel exhibits strongly negative double refraction, and is probably uniaxial; whilst young enamel presents positive double refraction. Adult enamel becomes positive on being exposed to a temperature of 800° C. Hoppe-Seyler (69), in one of his analyses, found the composition of the enamel of the newly born infant to be PO_5 3 Ca O O = 75·23, C O_2, Ca O = 7·18, Cl Ca = 0·23, PO_5 3 Mg O = 1·72. Organic compounds = 15·59. The enamel of adults contains only from one to three per cent. of organic constituents; but, on the other hand a large quantity of phosphate of lime. A remarkable feature is the presence of a small proportion of fluorine.

THE CUTICULA (*persistent capsule* of Nasmyth, 22; schmelzoberhäutchen of Kölliker) forms an extremely resistant investment not more than 1—2μ in thickness, covering the exposed portion of the teeth, and disappearing wholly when they are mature. When the enamel is present, the under surface frequently presents the impression of prisms in the form of small square areas.

Kölliker and others more recently have improperly applied the term enamel membrane to the cuticula, since it is developed with equal distinctness in teeth in which the enamel is absent, as for instance in the Pike.

In young teeth, examined when in the act of perforating the gum, the cuticula may be easily detached as a whole after slight action of hydrochloric acid. It may then be tinted with solution of nitrate of silver, which causes the appearance of figures similar to large epithelial cells. These, as the history of the development of the teeth shows (see this), are the cornified cells of the so-called external epithelium of the enamel organ, from which the cuticula is formed.

The chemical relations of the cuticula dentis indicate that it belongs to the category of horny substances. According to the statements of Kölliker (58), which I am able to corroborate, boiling water and mineral acids exert no action upon it, except that it is stained of a yellow colour by nitric acid. When boiled with caustic potash or soda, it softens, and when burnt yields a smell resembling that of horn. I have not been able to prove the presence of lime in the cuticle of man; small traces of

this substance could always be referred to imperfect purification of the membrane from enamel or dentine in contact with it; so that it is questionable whether it undergoes any calcification. Kollmann (67a) has recently admitted this, but offers no proof.

CEMENT (Zahn-kitt, *osteoid substance, cementum, cortex osseus, crusta fibrosa*).—The cement is a true bony structure essentially belonging to the periosteum of the alveolus, and in man and many of the vertebrates forms a thin investment to the fangs of the teeth. Intimately connected with the dentine, it commences as a delicate covering at the neck of the tooth, where the enamel ceases, and is thickest at the apices of the roots and in the depressions between the roots of the molar and bicuspid teeth. In the folded enamel and compound teeth the cement penetrates deeply in the form of a moderately thick layer between the projections of the crown, or serves as a connecting substance to the several toothlets; it is therefore situated for the most part external to all the other constituents of the tooth. The Pachydermata and others have also a special covering of cement, investing the whole crown of the tooth as a secondary formation (crown cement).

Both in its chemical and microscopical characters, cement is closely allied to bone. The lacunæ are for the most part large, and possess an enormous number of very long canaliculi, especially in the Cetacea. When the cement is extremely thin, however, they may be entirely absent, and it then presents on section a perfectly homogeneous and vitreous appearance. A similarly very hard lamella, destitute of lacunæ, occurs also in the outermost portion of the thicker layers of cement. Haversian canals, which sometimes open into the pulp cavity (Salter, 58) are found when the cement is thick, though it is rare to find any lamellated arrangement of the matrix.

Kölliker (58) has described peculiar cavities in the cement, which he considers to result from pathological processes. Sharpey's fibres also occur, and I have found the cement of the dog to be that best adapted to show them. The thick capsule-like investments surrounding one or several lacunæ, first noticed by Gerber (24) in the cement of the horse, are deserving of especial mention. These lacunæ, with their thick capsules, can be easily isolated in diluted acids, and may be

regarded as nests of osteoblasts formed in the process of ossification, and surrounded by thick sheaths of connective tissue.

Soft Structures of the Teeth.—The soft tissues belonging to the teeth include *the tooth pulp and the gums.* The former is the vascular and nervous matrix of the dentine, and the remains of the original tooth papilla. It constitutes also the model of the tooth on which the hard structures are formed like a cast, and therefore presents, in accordance with their difference in shape, an extremely various form. In old teeth, where the hard parts predominate to a remarkable extent, there remains only an inconsiderable residue of the pulp enclosing the cavum dentis, and in the human tooth it is reduced to a very slender thread containing a few vessels and nerves. The pulp is immediately connected with the periosteum and base of the alveolus by means of the foramina dentium.

In the incisors of the Rodents, which produce new dentine continuously, the pulp, even in adults, retains its original character, and its structure can there be best studied.

The principal portion of a good specimen of young pulp consists of indistinct finely fibrous connective tissue containing numerous cells, that recalls in many respects the mucous tissue of old atrophied umbilical cords, the elastic tissue only being absent. On account of the numerous large vessels which break up immediately beneath the surface into a plexus of capillaries of moderate width, the tissue appears quite cavernous. The external layer of the pulp is formed by a layer of large cells, of elongated form, and provided with numerous processes, called *Odontoblasts* (49, 59), which are arranged so as to form a kind of columnar epithelium.* These cells (see figs. 102, 103) are from 20 to 30 μ on the average in length, and about 5 μ in breadth. They are finely granular, and destitute of a membrane. The moderately large rounded or ovoid nu-

* The names formerly applied to them were dentinal cells (Elfenbeinzellen). Kölliker terms this entire layer of cells membrana eboris, because after the pulp has been withdrawn it usually cleaves to the inner surface of the tooth in the form of a continuous membrane-like layer.

cleus is usually contained in that end which is turned towards the pulp. In adults, as Boll (59) remarks, the form of the cells is very slender, whilst in young teeth they are more or less compressed. Three kinds of processes may be distinguished in these cells. The dentinal process, the pulp process, and the lateral processes. The dentinal processes constitute the above-described dentine fibres; it need here only be repeated that from one cell several dentine fibres are frequently given off (Boll counted as many as six). Such odontoblasts, with several dentinal processes, are broad at the end, directed towards the dentine, but as the processes pass on they gradually diminish to form dentinal fibres. The odontoblasts are intimately connected with each other by means of the fine short teeth which the lateral processes of all dentinal cells form. The short pulp process usually springs from the cell with a moderately broad base, and is constantly connected with one of the cells lying immediately beneath the membrana eboris, which last are usually somewhat larger and more darkly granular than those more deeply seated.

We are indebted to Boll (59) for first furnishing us with precise information in regard to the nerves of the teeth. He observed in the incisor teeth of the Rodents, after the pulp had been macerated for an hour in a solution of chromic acid containing $\frac{1}{32}$ per cent., a very large number of non-medullated extremely fine nerve fibres, which exhibited a silky lustre, and were gradually but directly continuous with the medullated fibres. If the observer is so fortunate as to preserve the membrana eboris in its natural connection with the pulp, which Boll sometimes accomplished by introducing a fine knife between the pulp and the dentine, after treatment with chromic acid, the extraordinary richness of these non-medullated fibres in the peripheric portions of the pulp becomes apparent. Preparations that have been teased out with needles show that the nerve fibres pass outwards between the odontoblasts in considerable numbers, and accompany the dentinal processes to which they are subjacent in the form of fine hairs. Boll was, however, unable to see the actual penetration of the nerve fibres into the dentinal tubuli, although their length and the direction they pursued rendered this probable.

The *gum* is distinguished from the other portions of the oral cavity by its vascularity and its large papillæ, which

again, like the papillæ fungiformes, are beset with small projections (Kölliker, 58). No glands appear to be present in them. Here and there small round heaps of pavement epithelium, frequently presenting the appearance of concentric lamellæ of horn, are met with, either imbedded in the substance of the gum, or occupying fossæ on its surface (Serres, 8; Kölliker, 58). The periosteum of the alveoli, which fulfils the office of periosteum, not only to the internal surface of the alveolus, but also to the cement, termed the Periodontium, is characterised by its softness. It contains but few elastic fibres, though I, with Kölliker (58), have found its nervous supply abundant.

Dentinal structures occur in large numbers, and present a great variety of form, amongst the Invertebrata. The teeth of the masticatory apparatus of the Echinus most closely resemble those of the Vertebrata. H. Meyer* states that they are composed of enamel fibres; this, however, is not quite accurate. The teeth of the Echinidæ are long, slender, slightly curved plates, which present a well-marked longitudinal ridge on their inner surface. The greater part of each tooth is formed by a radial lamina attached vertically to the surface of this ridge or keel. The radial lamina is moderately soft, and can be easily broken up into thin leaflets, which are again composed of elongated prisms somewhat curved at their extremities. The peripheric plate is considerably harder, and its prisms are much smaller and softer than those of the keel. Between these prisms, which in part run parallel to one another, and partly decussate in each plate, lie thin lustrous calcareous plates which often exhibit an extremely delicate plexus of fine anastomosing canaliculi. When treated with hydrochloric acid, the prisms dissolve with the disengagement of a large quantity of gas, and leave no organic residue. They appear, therefore, to be entirely composed of carbonate of lime. In their degree of hardness, in their size and chemical characters, they consequently differ remarkably from true enamel, and they do not possess the regular four or six-sided form, characteristic of the fibres of the latter substance. In Mollusks, Worms, and Arthropods the oral or gastric teeth are composed of chitine, which is sometimes impregnated with lime or silica. It may be said generally that the teeth amongst the Invertebrata are to be regarded as pure mineral

* Müller's *Archiv*, 1849, p. 191, *et seq.*

or epithelial structures (and are therefore analogous to the enamel), whilst in the lower Vertebrata they are chiefly composed of peculiarly modified and ossified connective tissue; in the higher classes of animals, which present the most complicated form of dentinal structures, an epithelial structure (the enamel) is again included in their structure.

DEVELOPMENT OF THE TEETH.—The genesis of the teeth in the human embryo commences, according to the observations of Robin and Magitot (46), at about the fiftieth to the sixty-fifth day. The margins of the jaw at the beginning of the third month form a slightly raised rounded ridge, the "*maxillary ridge*," which is most prominent in the lower jaw, and consists of a thickening of the embryonic connective tissue and epithelium of the mucous membrane of the mouth. This epithelium, with its vascular substratum resembling mucous tissue, constitutes therefore the matrix of the several constituents of the teeth, the *epithelium forming the enamel*, and the *mucous tissue the dentine and cement.*

The "*enamel organ*" is formed by a peculiar structure resulting from the growth and multiplication of the epithelial cells, which dip down into the mucous tissue. In a direction contrary to this there is then developed a papilliform process of the mucous tissue, the origin of the pulp and of the dentine. The two parts together constitute the rudiment of the tooth. When at a later period the connection of the enamel organ with the oral epithelium is interrupted, the rudiment of the tooth is enclosed in the alveolar border of the jaw on all sides, as in a capsule, by the sub-epithelial connective tissue. That portion of the connective tissue which immediately invests the rudiment of the tooth is usually termed the "*dental sac*," and at a later period forms the *cement*.*

ENAMEL ORGAN AND ENAMEL.—Near the end of the second month of fœtal life the margin of the jaw exhibits a slight

* Kölliker (58) calls the entire rudiment of the tooth enamel organ, papilla dentis, and the connective tissue investment of both, "dental sacculus," and distinguishes the latter again as "proper dental sacculus," a nomenclature which has little to recommend it.

longitudinal furrow, with rounded borders, termed the "dental groove." The epithelium of the oral cavity completely covers it, so that it is scarcely perceptible when the surface alone is examined. The two projecting borders of the groove are termed the "dental ridges" (Marcusen, 31), or "lips of the dental groove" (Dursy, 67). Soon, from the bottom of the dental groove, a narrow process of the oral epithelium dips into the subjacent mucous tissue, presenting on section the form of a short tubular gland, but in point of fact constituting an epithelial fold along the whole length of the jaw—the

Fig. 100.

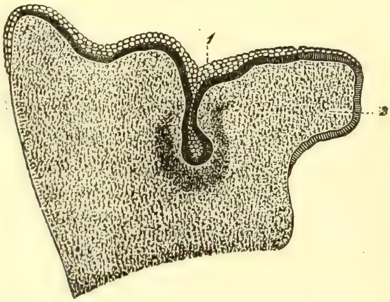

Fig. 100. Upper jaw of a fœtal sheep three centimeters in length. Vertical section, magnified 50 diameters, showing the enamel germ, with the semi-lunar rudiment of the dentine germ and dental sac in transverse section. 1. Dentinal groove. 2. Palatal process.

enamel germ of Kölliker (47). The primary dental groove, especially of the upper jaw, increases in size, and becomes entirely filled with oral epithelium. The epithelium also becomes extraordinarily increased in thickness on the two dental ridges, and in the deep groove between the lips and the margin of the jaw, especially in Ruminants (Kölliker, 47). At some points the enamel germ appears to descend perpendicularly from the base of the furrow into the subjacent tissue, but in other regions, especially in the neighbourhood of the incisors, it extends obliquely towards the median line, and consequently forms a larger or smaller angle with the dental groove.

The above account differs from that which I formerly gave, in recognising a *dental groove* in the vicinity of the subsequently appearing dental rudiment, and in not regarding this groove as a secondary formation caused by an hypertrophy of the epithelium. Kölliker (58) also describes a groove of this nature, and figures it with the enamel germ proceeding from its deepest part.* The statements of Marcusen (31) on the development of the teeth, which I

Fig. 101.

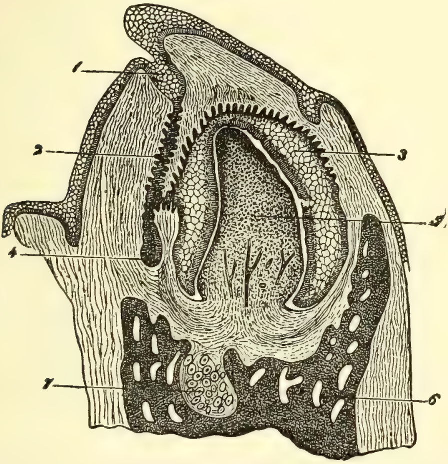

Fig. 101. Vertical section of the inferior maxilla of a human fœtus, measuring eleven centimeters from the vertex to the coccyx. Magnified 25 diameters. 1. Dental groove. 2. Remains of the enamel germ. 3. Enamel organ presenting externally epithelium, as also where it forms the enamel germ of the papillæ of the dental sacculus. 4. Secondary enamel germ; rudiment of the permanent tooth. 5. Dental germ. 6. Lower jaw. 7. Meckel's cartilage.

have already indicated as being the first that were accurate (49), require still to be followed out in further detail. Dursy (67) has very recently entered minutely into the description of the first occurrence of the dental groove, and has accompanied his statements with numerous illustrations. He considers it to be formed by an inequality in the growth of the margin of the jaw. He regards the enamel germ as resulting from the progressive development of the dental furrow and its epithelium, which, however, does not penetrate more deeply

* *Loc. cit.*, fig. 260.

into the margin of the jaw, but is rendered deeper by the increased elevation of the margins. I believe, however, that we must draw a distinction between the small primary dental groove with its epithelium and the true enamel germ. The latter is a secondary formation which, although proceeding from the epithelium of the primary dental groove, is yet distinguished from this, both by its sudden attenuation, by the difference in its direction, especially in the case of the incisor teeth, and by its microscopic characters. The epithelium of the dental groove, with the exception of the deepest layer, consists of large spherical or flattened transparent cells. The cells of the deepest layer are columnar, and are immediately continuous with the similarly formed cells situated at the periphery of the enamel germ, whilst the cells at the centre of the enamel germ are dark, granular, and round. Even at a later period we must still distinguish between the con tinuously enlarging dental groove and the enamel germ (see fig. 101.) Whether the enamel germ penetrates by its own growth into the blastema of the jaw, as I have described (49), or becomes more deeply imbedded in consequence of an increase in height of the dental walls, it will perhaps be difficult to decide. The small primary dental groove superjacent to this, which is not always present, may however be identified with the dental groove of Arnold (12) and the primitive dental groove of Goodsir. Both overlooked the enamel germ, and imagined the teeth to be developed from isolated papillæ in their dental groove.

A series of remarkable changes soon take place in the more deeply seated portions of the enamel germ, especially at the several circumscribed spots corresponding to the later developed milk teeth. The spheroidal cells forming the central part of the enamel germ begin to increase with rapidity, so that the germ becomes conically elongated, assuming the form of a club, which is continuous by means of a relatively narrow neck with the epithelial cone of the dental groove. Coincidently the dentine germ increases in a contrary direction, forming a club-shaped mass, and projects upwards into its base, so that the enamel germ comes to invest the dental papilla like a cap. The connection between the several portions of the enamel germ then become dissolved, probably in consequence of an increase of the connective tissue of the dental ridges, so that now a special division of the enamel germ, which since the time of Purkyné (14) has been *called the enamel organ*, cor-

responds to eachof the dentinal germs. Each enamel organ is thus composed of a strongly developed portion that surmounts the dentine germ like a cap, and a narrow cord of cells extending to the epithelium of the mouth—*the neck of the enamel organ,* which represents the remains of the primitive enamel germ (see fig. 101). The neck of the enamel organ disappears at a later period, whilst the two dental ridges coalesce with one another above. The rudiments of the teeth are thus surrounded on all sides by the loose connective tissue of the wall of the jaw.

Histological changes of a very remarkable character occur in the enamel organ, coincidently with the morphological changes that have been described above. The marginal cylindrical cells, where they are in immediate contact with the dentine, appearing as an epithelium covering it, become remarkably elongated, and form very regular six-sided prismatic bodies—in fact, the most beautiful and regular columnar epithelium found in any part of the animal body (see figs. 102 and 103). The sides of the cells present a distinct limiting membrane; but the protoplasm has no investment at the two extremities. At the base of the dentine germ, where it becomes continuous with the lateral walls of the enamel club, the cells become progressively shorter, until at last they assume a cubical form, and thus coat the portion of the internal surface of the enamel organ, or rather of the dental sacculus, which is turned away from the dentine germ. In accordance with Kölliker (47), we designate the elongated cylinder cells as the *internal* or *enamel epithelium,* and the remaining marginal cells as the *external epithelium* of the enamel organ. As far as the external epithelium reaches, the adjoining connective tissue exhibits tolerably regularly formed conical and vascular papillæ, which project into the epithelium, and correspond to the papillæ found in the remaining portions of the oral mucous membrane (see fig. 101.)

The complete continuity and concatenation of all these structures is most satisfactorily proved by a recent statement made by Dursy (67), which I am able to corroborate, that especially towards the neck of the enamel germ, similar papillary structures are present, which here pass without interruption into the papillæ of the gum. It is only

requisite to remark that they are much stronger, and developed at an earlier period, in the enamel organ than in the gum.

The small round cells of the enamel organ between the external and internal epithelium undergo at the same time a peculiar transformation. They acquire a stellate form, and unite with each other by their processes in the same manner as the cells of ordinary mucous tissue, which this part of the enamel organ so strikingly resembles that up to the time of Huxley (37) and Kölliker (47) they were always regarded as gelatinous connective tissue. The cells, however, lying in

Fig. 102.

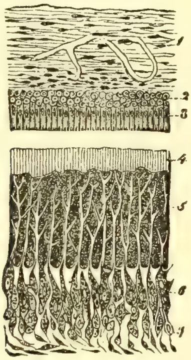

Fig. 102. Longitudinal section of a milk tooth from the fœtal sheep, carried through the margin of the dentine pulp and adjoining portion of the enamel organ. Magnified 200 diameters. 1. Dental sacculus. 2. External epithelium and stratum intermedium here united to the internal epithelium or enamel cells 3. after the disappearance of the enamel pulp. 4. Young layer of enamel detached from the enamel cells. 5. Dentine. 6. Odontoblasts. 7. Part of the dentine pulp.

immediate contact with the epithelium (stratum intermedium of Hannover, 39) retain their original form, and from these a continuous development of enamel cells, as well as of gelatinous epithelial tissue, appears to proceed. The enamel cells may be frequently seen to be in connection at their lower extremities with the cells of the stratum intermedium, so that a multiplication of the enamel cells from the cells of this stratum in

the direction of their length may be admitted to occur (see fig. 103, 2). The jelly of the enamel organ (enamel pulp) possesses only a transitory and mechanical significance, occupying the space subsequently required by the growing tooth, Nevertheless, before the formation of the enamel is completed. both the epithelial and gelatinous tissue and the stratum intermedium undergo atrophy. The outer and inner epithelia consequently again come into close apposition (see fig. 102); the latter is entirely used up in the formation of the enamel, and in teeth examined just at the period of eruption we can only detach from the enamel a membrane composed of one or more layers of very flat epithelial cells, which clearly represent the outer epithelium with a larger or smaller amount of the stratum intermedium. As soon as the eruption of the tooth is effected, these cells become horny, and form the cuticula dentis.

This conversion so remarkable in a histological point of view, of a portion of the epithelial cells of the enamel organ into stellate gelatinous tissue, finds an analogy, according to Kölliker (58), only in the cells of the external investment of the egg of the Perch. I have myself occasionally met with a similar metamorphosis of the epithelial cells in the Graffian follicles, but never occurring in so regular a manner. Renewed investigations, notwithstanding the objections raised by Kölliker (58) and Kollmann (67 a), compel me to adhere to the view I have above expressed of the nature of the cuticula dentis. Its tenuity cannot be considered as an objection, especially if, as I am now inclined to believe with Hertz (52), the external epithelium is alone to be regarded as the basis of the cuticula.

The formation of the enamel is purely and exclusively referrible to the enamel epithelium, the enamel prisms resulting from the *direct calcification* of the long cylindrical cells. The intimate connection of enamel cells with small portions of the enamel prisms, which remain adherent to the cells in the form of processes, is in the first place in favour of this view (see fig. 103, 3). Again, the limit to which the calcification extends is not bounded by a straight line, but is very irregular, a circumstance that is opposed to the idea of a calcification of any secretion formed by the enamel cells. If young enamel be treated with diluted acids, the enamel prisms swell up to some extent, and

reassume the form of the original columnar cells, and the distinct membranous investment of the longer sides comes into view. The disappearance of the nucleus in such calcifications and metamorphoses of cells is so common, that there is nothing remarkable in its absence in those of the enamel.

Fig. 103.

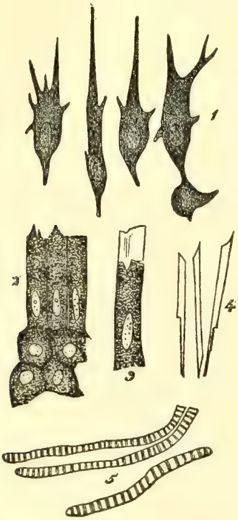

Fig. 103. Highly magnified. 1. Various forms of odontoblasts. 2. Three enamel cells, with a few cells of the stratum intermedium attached ; two enamel cells exhibit Tomes' processes. 3. An enamel cell, with a small portion of enamel. 4. Fragments of enamel fibres from young and still soft enamel (acicula). 5. Old enamel fibres with transverse striæ.

Kölliker (58) has recently so far inclined towards the view propounded above, that he appears inclined to explain the formation of enamel in the same sense as Schwann (23), who held that the enamel cells continued to grow at their free extremities, and that the new growth underwent continuous calcification, Hertz (52) and myself (49) transfer the growth of the cells to the nucleated extremity directed towards the stratum intermedium, which is more in accordance with the facts observed, and with the general mode of increase of cells ; for the nucleus, with the immediately surrounding protoplasm, is

always that of part of the cell from which the phenomena of life radiate with the greatest activity, whilst the peripheric portions constantly, on the other hand, have a tendency to death or to transformation into intercellular substance, etc. In favour of the same view also is the remarkable circumstance, that in all elongated columnar cells, with one nucleus in their interior, the latter is constantly found to occupy the attached and never the free extremity.

From the foregoing remarks, then, it appears that enamel is to be regarded as the *petrified dental epithelium*, and that its essential part corresponds to the mucous layer of the oral epithelium, whilst the cuticle, though perhaps by a secondary metamorphosis, is associated with the horny structures.

The delicate membrane described by Huxley (37), in his account of the structure of the teeth, which can be raised with tolerable facility from the surface of the developing enamel after it has been subjected to the action of hydrochloric acid, is the youngest layer of the enamel as yet but slightly impregnated with mineral constituents (Tomes, 29). The foraminated appearance of the membrane is in favour of this view. The enamel cells first undergo petrifaction in their investing (external) zone, the axial portion of the protoplasm retaining its softness for a time, and in isolated cells forming a kind of process (Tomes' Process of the Enamel Cells (49), (see fig. 103, No. 2). As a consequence of this the youngest layer of enamel must necessarily exhibit a number of foramina, corresponding to the "Processes" of Tomes. Huxley correctly identifies this membrane with the *membrana præformativa* of Raschkow, but erroneously considers the cuticula dentis to proceed from it. Raschkow described a thin homogeneous membrane investing the dentine germ, which was regarded by Todd and Bowman, and by Kölliker, as a basement membrane of the dental papilla covering the surface invested by epithelium (enamel cells). Huxley (37) and Kölliker also describe a basement membrane between the mucous membrane and the external epithelium. Such a membrane is, however, only discoverable when the enamel cells have attained a certain stage of development, and have already begun to be calcified. If this membrane, which exhibits the characteristic foramina of Huxley's membrane, be raised by the action of hydrochloric acid, no other homogeneous basement membrane can be demonstrated on the dentine germ.

The papillary projections of the dental sacculus directed towards

the enamel organ afford an explanation of many of the peculiarities in the course of the enamel fibres which have been mentioned above. In the first place, the fine transverse striæ which run in a circular direction around the external surface of the enamel are directly referrible to the papillæ. For if, towards the end of the formation of the enamel, the enamel pulp disappears, and the external and internal epithelial cells again come into contact with each other, the papillary processes make their mark on the enamel membrane, and naturally also on the product of its calcification, the enamel. The transverse elevations of the latter are thus of precisely the same nature as the well-known fine striæ of the nails. Moreover, since the greater part of the enamel is formed before the enamel jelly has disappeared, and therefore at a time when the enamel membrane already exhibits the impressions of the papillæ, we may reasonably refer many peculiarities in the course of the enamel prisms, especially their decussations, spiral course, and undulations, as well as their optical characteristics, to the same cause.

DENTINE AND CEMENT.—As Dursy (67) maintained, the first germ of the dentine appears in the dental sacculus as a dark semi-lunar area at the bottom of the dental groove—that is to say, of the enamel germ—coetaneously and continuously with which it is developed along each half of the jaw (see fig. 100). At certain points corresponding to the position of the subsequent teeth the young structure develops in the form of papillæ projecting against the enamel germ, whilst the remainder atrophies. The two horns of the semi-lunar mass (seen in section) extend, from the base of the dental papilla, some distance upwards, and embrace the dentine germ and the enamel organ. This constitutes the first trace of the *dental sacculus*, which at this period consists of tissue somewhat richer in cells and vessels than the mucous tissue of the dental groove. The dental sacculi are only well defined at the earlier periods of the formation of the tooth. When the process of development is more advanced, it is impossible any longer to distinguish a capsule-like layer of connective tissue around it. Moreover the dentine germ is only a special division of the mucous tissue of the dental groove, unusually rich in vessels and cells. After it has attained a certain size, the *odontoblasts* above described develop from the cells lying at the periphery,

and we soon recognise a solid shell of dentinal bone superimposed on the dentine germ, like a cap. The histological formation of the dentine is precisely similar to the ordinary process of ossification.

Whilst the peripheric portions of the odontoblasts constantly undergo metamorphosis, with disappearance of their nuclei, into a gelatigenous matrix which subsequently undergoes calcification, their centric portions penetrate the hardened mass in the form of longer or shorter threads, and represent the first rudiments of the dental fibres. The lateral processes of the odontoblasts occasion the numerous anastomoses of the dental fibres, or of the dental tubuli. Every odontoblast communicates with the more deeply situated and successively enlarging cells of the young pulp by means of its pulp process, so that when an odontoblast is calcified up to the base of the fibre, another occurs in its place without any interruption to the continuity of the fibre. Hence every dental fibre, with its anastomoses, must be regarded as formed of several continuous odontoblasts. The layers of matrix immediately surrounding the fibres undergo conversion, as appears from their chemical characters, into elastic tissue, and form the dental sheaths of Neumann. It has not yet been ascertained whether they also undergo calcification. *Thus it appears that the dentine, with all its constituents, proceeds from odontoblasts that have become metamorphosed in their form and chemical composition.*

No further detail respecting the process of dentinification need here be entered upon, since, so far as regards the osteoblasts, it presents the most complete analogy to that of ossification (see p. 135).

This analogy is still more close in regard to the formation of the cement, in which the histological processes are identical with those of intra-membranous ossification. The matrix of the cement is the loose myxomatous connective tissue of the dental alveoli which immediately surrounds the teeth, and so far we may thus consider the dental sacculus to be the matrix of the cement. A special cement germ, such as has been described by Robin and Magitot (46), in certain species of

animals, as in the Ruminants, Pachydermata, etc., does not, according to my observations, exist.

In animals with successive teeth, as Kölliker (47) has demonstrated, a process is found, even at the period of the first appearance of the enamel organ at its median side, which is either given off from the neck of the enamel germ or from a still deeper part, and becomes the enamel organ of the persistent teeth (see fig. 101). On the other hand, no trace of a dentine germ for these latter teeth is at this period visible.

Hertz (52) mentions the occurrence in several preparations of a second inflection of the oral epithelium superjacent to the enamel germ of the milk teeth, which he is inclined to regard as the enamel germ of the persistent teeth. Nevertheless there is much here that requires elucidation, especially in respect to the formation of the three molars of man, which, as is well known, are not preceded by milk teeth.

The processes occurring in second dentition have been very recently minutely investigated by Kehrer (56) and Lieberkühn (57). As the persistent tooth projects, the alveolar wall dividing it from the milk tooth sacculus undergoes absorption, and with this there immediately occurs a process of cell proliferation in the sacculus of the milk tooth, under the influence of which the fang, with the formation of the so-called Howship's lacunæ, is absorbed as far as the crown. The young granulations in the meanwhile take the place of the fang of the milk tooth. The remains of the pulp of the milk tooth unite with the granulations now causing erosion, which, however, are themselves compressed by the growing tooth, that pushes the remains of the milk tooth so far forward that it falls out. No obliteration of the vessels of the milk tooth occur. The true mode in which absorption is effected, the formation of the lacunæ of Howship, is no better understood here than in the case of the absorption of bone. Kehrer believes, from finding chalk granules in the protoplasm of young cells, that the amœboid cells of the granulations destroy the dental tissue by a kind of mining process, effected by their pseudopodia.

The Gubernaculum of the second set of teeth, already described by the older anatomists, consists, according to the observations of Lieberkühn, only of a cord of connective tissue, which traverses the alveolus in order to conduct the nerves and bloodvessels to the dental sacculus. It has no relation to the process of dentition itself.

Our knowledge of the development of simple teeth consisting

only of cement, dentine, and probably also always of cuticle, requires revision. According to the statements of Owen (25), these neither possess an enamel organ, nor form a closed dental sacculus.* We possess no accurate information of the relations of the oral epithelium. Probably there is here, as Leydig (36) describes in several species, as, for example, in the Anguis fragilis, a thin covering to the freely projecting dental papilla, which subsequently becomes the horny cuticle. In accordance with a more recent investigation of Leydig (62), the crowns of the teeth, which, however, have no investing enamel, originate in Salamandra maculosa, in several dental sacculi which lie at the bottom of the "epithelium of the jaw." The fangs are developed from the subjacent connective tissue. Leydig considers the substance of the dental crowns to be a cuticular formation.

The simple horny teeth do not differ in their formation from the ordinary papillæ of the oral mucous membrane possessing a strong horny investment. Nothing is at present known of the mode of development of the more compound forms occurring in Ornithorhyncus and others.

Accurate knowledge of the dental tissues, and of their development, commences with the works of Purkyné and his scholars, Fränkel (13) and Raschkow (14). Leeuwenhoek (2) had indeed previously seen the dental canaliculi, and, like J. Hunter (4), had recognised the cement as a distinct substance, the discovery of which is ordinarily attributed to Blake (5) and Tenon (6); still it is only from the time of Purkyné that the knowledge of this subject has become common property. The enamel fibres have been described by many from the time of Malpighi. Retzius (19) and Hannover (39) gave the most accurate description of the structure of the dentine and enamel, especially with regard to the various lines and markings upon and in them, and the course of the canaliculi and enamel fibres. Nasmyth (22) and Erdl (27) first described the cuticle, and Czermak (33) the interglobular substance. We are indebted to E. Neumann (48) for the demonstration of the dental sheaths,

* Owen, moreover, claims enamel for many animals, in which it does to exist, as, for instance, the frog.

and to F. Boll (59) for following out the dental nerves in their further course. In recent times, Tomes (29, 40) has most successfully worked at the finer points of dental structure, and by demonstrating the dental fibres first opened the way to a correct interpretation of the nature of the dentine; previously to him, as by J. Müller (16) and Lessing (28), the dental canaliculi were regarded in reference to their contents precisely in the same light as the lacunæ of bone. Tomes also furnished numerous and valuable contributions to the comparative anatomy of the teeth. On the latter subject, however, the important work of Owen (25) constitutes the principal authority, but those of Erdl, Hannover, Huxley (37), Agassiz (15), F. Müller, and Henle (20) may also be enumerated. Amongst the points in the histology of the teeth still requiring elucidation the structure of the enamel and the final terminations of the dental nerves deserve to be mentioned. If we except the works of Arnold (12) and Goodsir (21) (who however considered that the teeth originate from free papillæ at the bottom of an open dental groove) as constituting the first comprehensive investigations towards the elucidation of the genesis of these structures, those of Marcusen (31), Huxley (37), and Kölliker (47, 58), have proved of the highest value. Marcusen gave the minute details of the primary origin of the teeth quite correctly, and referred the enamel to the oral epithelium, as Huxley also has always maintained; and Kölliker's accurate investigations have placed the fact beyond doubt. Purkyné and Raschkow had already demonstrated the enamel organ, Schwann (23) the enamel cells and odontoblasts, and Lent (38) and Kölliker (58) the dentinal processes of the latter. The external epithelium has likewise been correctly described and explained by Marcusen. All later observers, Nasmyth, Huxley, Natalis, Guillot (44), Todd and Bowman (35), Robin and Magitot (46), notwithstanding that they described this epithelium with great minuteness, have furnished us with no new information respecting it. Dursy (67) has followed the papillary processes of the dental sacculus, together with the intervening depressions of the external epithelium which frequently appear as glandular structures belonging to the latter, as far as the enamel germ, and from thence on to the papillæ of

the maxillary mucous membrane. To judge from his description and illustrations, Hérissant (3) must have already seen the papillæ, which he considered to be glands for the secretion of enamel. Their importance in the formation of enamel has not been sufficiently estimated. Most of the contested points await their elucidation from an accurate knowledge of the histogenesis of the dentine and of the enamel. Kölliker (58), with whom Hertz (52) is in accordance, so far as regards the dentine, and Kollmann (67a), in regard to the enamel, still considers both substances as a hardened excretion of the odontoblasts or enamel cells; whilst Tomes, Hertz, and Wenzel (66) (in the continuously growing incisors of Rodents), in regard to the enamel, and Boll recently in regard to the dentine, agree with the view given in the text. Kollmann admits also a membranous investment to the free ends of the enamel cells; this continuous layer forms the membrana præformativa, and at a later period, when calcified, the cuticula dentis.

In the following account of the literature of the subject, besides the most recent works, only those are mentioned which have given either extended and complete descriptions, or have furnished some new facts. References to the older literature are well given in Hérissant, Henle (26) and Robin, and Magitot.

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CHAPTER XVI.

THE INTESTINAL CANAL.*

By E. KLEIN AND E. VERSON.

A. Oral Cavity, by E. Klein.

The mucous membrane of the oral cavity in man begins at the lips as a direct continuation of the outer integument.

Three anatomically different parts† can be distinguished in it : a cutaneous, a transitional, and a muco-membranous portion.

The transitional portion is marked off from the cutaneous portion by the outer border of the red lips, and from the muco-membranous portion by the most prominent part of the convexity of the lips, so that when the mouth is closed the red visible portion of the lips represents the transitional portion.

The cutaneous portion is covered by a thin epidermis consisting of one or two layers of flattened epithelium intimately fused with one another ; subjacent to this is a thinner mucous layer, in which are small rounded cells containing relatively large nuclei.

The cutis internal to this is composed of fasciculi of fibres, which decussate with one another, the principal ones being directed towards the free border of the lips. The fibres which form these fasciculi consist, for the most part, of fine connective

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* The account given in this section rests on investigations which the authors have undertaken in my laboratory for this work.—S. Stricker.

† E. Klein, *Zur Kenntniss des Baues der Mundlippen des neugebornen Kindes*, "On the Structure of the Oral Lips of the newly born Child;" *Sitzungsberichte der k. k. Akadem. der Wissenschaften in Wien*, December Heft, 1868.

tissue fibres, between which isolated or plexiform fibres of elastic tissue run.

The surface of the cutis directed towards the epidermis presents rows of cylindrical or conical small vascular papillæ standing in tolerably close proximity with one another, and projecting into the rete mucosum to about half its thickness. The nervous and vascular trunks proceeding from the subcutaneous tissue, or from the muco-membranous and transitional portions, make their way between the muscular fasciculi, and curve at nearly right angles in the cutis. Hairs and sebaceous follicles are distributed in moderate number at nearly equal distances, and at various depths in the tissue. The hair follicles of the upper lip are directed obliquely downwards at their base, those of the lower lip upwards. The points of distinction between the transitional and the cutaneous portions of the lips are the absence of hair follicles and sebaceous glands in the former; the presence of wedge-like fasciculi of the orbicularis oris in it, which reach nearly to the epithelium; the much greater transparency of its superficial cells; the arrangement of its morphological elements generally; and, lastly, its far more abundant supply of bloodvessels.

The epithelium, as a whole, remains at a short distance from the last hair follicles, as deep as at the cutaneous portion, but beyond this rapidly increases in thickness. The superficial cells are much flattened, intimately fused with one another, and without apparent nuclei; but those which are rather deeper, though still tabular, become somewhat elongated, and possess a well-defined and usually elongated nucleus. The cells of the middle layers increase as they are more deeply situated in their vertical diameter, and become proportionately narrower, with round nuclei; the deepest cells are round, with relatively large spheroidal or irregularly shaped nuclei.

The chief fibrous layer of this transitional portion is composed of broad highly refractile fibres, capable of resisting the action of acetic acid, and united into plexiform fasciculi. The fasciculi separate from each other at many points to permit the passage of the horizontally coursing vascular trunks, which are here very numerous.

The thickness of this layer is least where the hair follicles cease; from this point it gradually increases, and is thickest at the commencement of the muco-membranous portion. Its surface is beset with very numerous thin and elongated papillæ, which are frequently clavate, oblique in direction, and vascular.

Between the fibrous layer and the submucous tissue of the muco-membranous portion, and near the commencement of the latter, are situated the coronary artery and vein. These give off larger and smaller branches to form a plexus beneath the epithelium from which the vessels for the supply of the papillæ arise.

The third part of the lip, the muco-membranous portion, possesses an epithelium that far exceeds in thickness that of the two above-named portions; but if this be followed over the fold of the lip, it will be found again quickly to diminish. It presents the several layers characteristic of laminated flattened epithelium; the most superficial layers consisting of flattened tubular cells, with a flattened and for the most part elongated, though occasionally spheroidal, nucleus; subjacent to these are cells that at first are of greater breadth than depth, but become in the deeper layers more and more polyhedric, till they are finally succeeded in the deepest layers by cells which are arranged in the form of palisades.

Many of these cells are ribbed, or exhibit thorn-like projections, by virtue of which they are connected with each other by a dentated suture.

The tissue of the mucous layer is composed of finer and coarser fibres. The former are either united into fasciculi, or run, in the form of fine isolated or paired elastic fibres, sinuously between or in many spiral coils around the decussating and plexiform fasciculi. Besides these, broad, highly refractile, strongly looped fibres occur.

Wherever the fibres of the membrana mucosa pursue any definite general direction, it is horizontal, and directed from one side of the lip to the other. Moreover, numerous fasciculi pierce the muscular layers to reach the subcutaneous tissue of the transitional portion. Near the muscular fasciculi the tissue undergoes alteration, becoming less dense, and the mucous membrane passes into submucous tissue.

The membrana mucosa is beset with conical, usually un-

divided, but occasionally bifid or trifid papillæ, which often, coming into contact at their wide bases, project into the epithelium; the longest of these (0·525—0·63 of a millimeter in length) are situated at the commencement of the muco-membranous portion posteriorly; coincidently with the diminution in the thickness of the epithelium they likewise become shorter, and do not exceed half the depth of the epithelium.

The epithelial cells covering the papillæ are arranged in an imbricated manner, and are much flatter than the cells situated on the same level between the papillæ. Corresponding to the first two or three rows of papillæ situated at the commencement of the muco-membranous portion, the epithelial surface presents a small elevation; and in newly born children the papillæ of this part of the lip, and those at the angles of the mouth, project as much as one millimeter beyond the lower plane of the epithelium.

The glands that are situated in the submucous tissue of the muco-membranous portion make their first appearance behind the most prominent portion of the convexity of the lip, and, indeed, at that point where the epithelium begins to be constant in thickness.

They constitute acinous glands that are essentially similar to the salivary glands. Our knowledge, however, is not sufficiently advanced to enable us to state that they present those characteristics of the salivary glands which have been the subject of recent investigation. They open on the surface of the mucous membrane or epithelium by means of small excretory ducts. Each of these is a canal bounded by a structureless membrane, in which the laminæ of tesselated epithelium only extend to the depth of the epithelial layer generally; beyond this it is lined by a single layer of cylindrical epithelium. After pursuing a spiral course obliquely through the membrana mucosa it gives off numerous branches, which frequently divide and terminate in the individual acini. The acini belonging to a large branch are united into a lobule by the fasciculi of the submucous connective tissue, and these again are formed into lobes. The fasciculi and fibres which limit a lobulus or a lobe, and in the meshes of which the several acini are imbedded, are continued as a sheath to the excretory duct in its passage

through the mucous membrane. The plexiform tissue composed of fasciculi of fine connective tissue fibres belonging to the submucous layer, and which, together with delicate frequently coiled elastic fibres, forms the framework of the gland, is at the same time the support of small nerves, and of a close system of capillaries which surround the acini.

In this tissue there lie, partly isolated amongst the fine fibres of the connective tissue fasciculi, partly accumulated in larger numbers near and around the acini, lymph corpuscle-like cells, as well as large, coarsely granular, irregularly shaped masses of protoplasm, which usually contain a small nucleus.

Sebastian* counted fifty-seven glands in the lower lip alone; in other cases there were thirteen and twenty-one of these glands. Their diameter amounts from $\frac{1}{2}$ to $1\frac{1}{2}$ millimeter, or more; and as a rule their size increases in proportion to the smallness of their numbers; they are largest in children, and diminish as age advances.

In the lower lip of the child† they are arranged in four or five consecutive rows. Their number rarely exceeds three in the upper lip, and they are altogether absent at the angles of the mouth.‡ I find that in the child they are larger in the lower than in the upper lip. Besides the glands, large vessels and nerves are also found in the submucous tissue of the muco-membranous portion, the latter for the most part running in a vertical direction, giving off smaller branches to the mucous membrane, which again subdivide, and may be followed to the immediate vicinity of the epithelium.

The nerves of the papillæ have not been accurately investigated. According to W. Krause, the so-called terminal bulbs—structures respecting the nature of which there is still some doubt—are found in the lips of many Mammals.§

Kolliker|| has observed in the papillæ of the lips, but only of that part which is visible when the mouth is closed, tactile corpuscles, and

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* Sebastian, *Recherches anatomiques, physiologiques, pathologiques, et semeiologiques sur les Glands Labiales.* Gröningen und Bremen, 1842, 4to.

† E. Klein, *loc. cit.*

‡ Henle, *Splanchnologie*, p. 138

§ W. Krause, *Die terminalen Körperchen.* Hanover, 1860.

|| *Zeitschrift für wissenschaftliche Zoologie*, Band iv., Heft i. p. 43.

in one instance he found nerve coils in the small papillæ, and at the bases of the larger. Gerlach* also ascribes tactile corpuscles to the papillæ of the borders of the lips.

The fasciculi of the musculus sphincter oris are intercalated between the submucous tissue of the muco-membranous portion and the subcutaneous tissue of the cutaneous portion. According to C. Langer,† the muscular fibres of each side have three points from which they radiate towards the median line, namely, the angle of the mouth, and the two musculi incisivi; from the angles of the mouth the fibres arranged in a laminated manner pass to the lips, one portion terminating without crossing the median line in the cutis of its own side, another passing beyond this to terminate in the skin of the lip on the other side, and, finally, a portion of the fibres attaching themselves to the incisor processes of the bones on the same side. Moreover, according to Langer, the fibres of the sphincter penetrating the cutis lose themselves amongst its plexiform fibres. Woodham Webb ‡ has likewise, some time ago, demonstrated the presence of transversely striated muscles in the lips of Man, from which extremely delicate fasciculi extend into the papillæ of the cutis, and are there lost. It may be shown by carefully made sections that a portion of the muscular fibres which Langer and Woodham Webb considered to penetrate the cutis belongs to a peculiar system of muscular fibres (compressor labii) which arise in the spaces intervening between the first 5—7 consecutive rows of hair follicles, arrange themselves in the subcutaneous tissue in four or five fasciculi, traverse, forming slight curves, the fasciculi of the sphincter, and at their entrance into the muco-membranous portion, that is to say, into the submucous layer of this portion, every two or three fasciculi decussate alternately, in order finally to penetrate

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* *Handbuch der allgemeine und speciallen Gewebelehre des menschliches Körpers. Mainz*, 2 Aufl.

† *Ueber den Musculus orbicularis oris, Wiener Medicinische Jahrbücher*, Heft ii.; *und Zeitschrift der Gesellschaft der Aerzte*. Wien, 1861.

‡ "On Striated Muscular Fibres in the Skin of the Human Lip," *Quarterly Journal of Medical Science*. London, 1857, January, Vol. v., p. 89, plate vii., fig. 16.

the mucous membrane itself in a fan-like manner, or, more rarely, to enter its transitional portion.

The several muscular fibres, both of the muco-membranous portion as well as of the cuticular portion, may be followed into close proximity with the epithelium, or to the base of the papillæ. The sarcolemma is continued for a short distance between the fibres of the membrana mucosa, or of the cutis, in the form of delicate fibres. In the cutaneous portions the muscular fibres partially decussate at the base of a hair follicle, whilst elsewhere they may be followed on the wall of the hair follicle to near the rete mucosum.

This muscle in the lower lip is more strongly developed near the middle line than at the sides; but in the upper lip, in which it is usually more feebly marked, the opposite obtains. Laterally the fibres are directed radially towards the oral opening, and the area embraced by its origin and insertion is larger.

At the angles of the mouth the mucous membrane rests upon the inner surface of the buccinator, and extends, as the mucous membrane of the cheeks, as far back as to the anterior border of the vertical ramus of the lower jaw, without presenting any important variation in its structure. Its epithelium is of the same thickness and structure as that already described as covering the muco-membranous portion, except that the number of ribbed cells in the middle layers of the mucous membrane of the cheeks is much greater than in that of the lips.

The form of the papillæ which project from the Memb. mucosa into the epithelium is irregular; they are often conical, with elongated apices, or with their points prolonged in a filiform manner. At their bases they are relatively broad. Their height varies, sometimes amounting to half the depth of the epithelium, sometimes scarcely exceeding its lower boundary line. The Memb. mucosa is most dense beneath the epithelium, and in it the same arrangement of the elements may be recognised as in that of the lips. Towards the buccinator muscle it becomes more loose. Its fasciculi stand in the same connection with those of the subcutaneous tissue as in the case of the lips.

The glands of the mucous membrane of the cheeks (Glandulæ buccales) are thinly scattered, and are only to be found at considerable distances from each other; near the point where

Steno's duct opens they also form a series of glands known as the glandulæ molares.* According to Ward, they are from two to four in number, are situated between the masseter and buccinator muscles, and are larger and composed of more lobules than the remaining glands of the oral mucous membrane.

At the point where the lips are reflected upon the anterior surface of the jaws, the mucous membrane at the middle line, both above and below, forms a small duplicature, termed the *frœnum.*

The epithelium of the mucous membrane is here thinner than elsewhere; the papillæ are also smaller and less numerous; the mucosa itself is not distinguishable. The vessels are relatively numerous, and it contains a considerable number of fine irregularly coursing elastic fibres.

That portion of the mucous membrane which covers the alveolar processes of the jaw, and surrounds the necks of the teeth, passing anteriorly into the mucous membrane of the lips, posteriorly at the root of the oral cavity into that of the hard palate, and below into that of the floor of the mouth, is named the *gum* (Gingiva).

The *gum,* on account of the abundance of tendinous fasciculi it contains, is denser and tougher than the mucous membrane of any other part of the mouth; it is intimately adherent to the bone in consequence of the direct prolongation of the tendinous fasciculi of the periosteum into the mucosa.

The epithelium of the gum is composed of laminæ of tesselated cells, amongst which are exceedingly well-marked ribbed cells. The superficial cells are strongly flattened; those more deeply situated become thicker, and possess strongly defined ribs. The deepest cells are cylindrical, with conical external extremities.

The *papillæ of the mucosa* of the gum are all relatively broad at their bases, of unequal height, with conical or rounded external extremities, which are sometimes simple and sometimes divided.

The tissue of the mucosa is tough, and is composed of broad

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* N. Ward, art. "Salivary Glands," in Todd's *Cyclopædia of Anatomy and Physiology*, Vol. ii., p. 422.

fasciculi of connective tissue, the fibres of which run in a straight direction. It also contains a not inconsiderable number of finer or coarser closely coiled elastic fibres. In the mucous membrane of the gum, three separate fibrous layers may be distinguished : *a.* Fasciculi of fibres which run in a horizontal direction from right to left parallel to the surface, and then break up into smaller fasciculi that, after frequently decussating, reunite into coarser bundles ; these predominate on the anterior surface of the alveolar process over the two following sets of fibres. *b.* Fasciculi which, proceeding from the periosteum of the alveolus, cohere in large bundles, and immediately again break up in a fan-like manner whilst coursing towards the epithelium, either from before backwards or from behind forwards. On approximating the epithelium, the smaller fasciculi break up into isolated fibres, which, running apparently between the cells, penetrate the deepest epithelial layers. *c.* Lastly, there are fasciculi which run in a vertical direction from above downwards, or from below upwards, and in other respects resemble those described under *a.*

At the posterior part of the gum of the upper jaw, where this passes into the mucous membrane of the hard palate, all three sets of fibres frequently decussate.

The nerves of the mucous layer of the gum are not numerous.

The mucous membrane of the *hard palate* presents many differences in structure from that of the gum. The laminated pavement epithelium, which at first is thinner than that on the gum, gradually increases in depth posteriorly. The number of ribbed cells contained in its middle layers varies at different points. The papillæ of the mucous membrane projecting into the epithelium are not nearly so numerous at the commencement of the hard palate as on the gums. The median papillæ, especially near the foramen incisivum, are frequently observed, through tracts of considerable extent, to be indicated only by sparingly distributed slight depressions of the deep surface of the epithelium. Posteriorly the papillæ increase somewhat in number and height, although even in some parts of the posterior third of the hard palate they are not much larger than quite anteriorly.

The mucous layer subjacent to the epithelium is thinnest

over the anterior third of the median line; more externally it is generally thicker, attaining its maximum posteriorly.

The fasciculi, as a general rule, run as if they radiated from the arch of the alveolus of the upper jaw towards the median line of the hard palate. In the anterior part of the mucous membrane, consequently, they run from before backwards, but more posteriorly from side to side.

Their constituent elements consist anteriorly, for the most part, of broad fibres, which form a close plexus beneath the epithelium; but at a plane somewhat deeper there is a loose network of connective tissue, constituting a submucous layer, the fibres of which are more densely matted as they approach the bone, and finally become continuous with the periosteum. In the middle and posterior thirds the mucous membrane beneath the epithelium is looser in texture, but at a deeper level the fasciculi of connective tissue are woven into a compact felt, and separate in the submucous tissue from one another to form meshes of variable size. Laterally the submucous tissue contains fat cells which are most abundant in the middle third.

The vessels and nerves run in the submucous tissue of the middle line and lateral portions of the anterior third, the former pursuing for the most part a longitudinal, the latter a transverse direction. The more externally the part examined is situated, the more numerous are the nerves, the small branches of which form arches in the mucosa. In the middle part of the hard palate, and in the first instance laterally, acinous glands occur in the submucous tissue, which are isolated in front, but subsequently grouped either into a single or (towards the posterior and external portion of the middle third) into two longitudinal rows. Szontagh counted 250 glands in the hard palate.*

After the mucous membrane of the oral cavity has covered the hard palate, it forms posteriorly a muscular fold, the *velum palati*, or soft palate, which presents in man a conical median prolongation, the *uvula*, and is also continuous with the mu-

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* Szontagh, *Beiträge zur feineren Anatomie des menschlichen Gaumens*, "Essays on the Minute Anatomy of the Hard Palate in Man;" *Sitzungsberichte der k. k. Akademie der Wissenschaft. zu Wien.* März Heft, 1866.

cous membrane of the nasal passages. The mucous membrane of the soft palate is continued laterally and downwards as the arcus palato-glossus into that of the root of the tongue, and as the arcus palato-pharyngeus into that of the pharynx.

In newly born children the apex of the uvula and the immediately adjoining parts are covered with tesselated epithelium, whilst the posterior or upper surface is invested with a laminated cylindrical and ciliated epithelium. The most superficial cells are here beset with short hair-like processes, present a conical form, with the apices directed away from the surface, and contain rounded or laterally flattened nuclei; subjacent to these are fusiform or elongated oval cells, and still deeper lie others that are flattened at the sides by mutual pressure.

The transition of laminated pavement epithelium into laminated cylindrical and ciliated epithelium is effected by a diminution in the number of the middle layers of the cells, which are not arranged as before, with their shortest diameter perpendicular, but parallel to the surface; and by the disappearance of the most superficial flattened cells, which are replaced by cylinder cells, that increase in number in proportion to their distance from the apex of the uvula.

On the posterior surface of the uvula and of the soft palate of the new-born infant there may moreover be found numerous isolated areas, presenting well-developed pavement epithelium, as well as transitional forms between the laminated cylinder and pavement epithelium. In adults* a laminated pavement epithelium exists both on the anterior and on the posterior or superior surfaces of the uvula and soft palate, and this may be divided into two layers, of which the cells forming the deeper are smaller than those of the superficial.

The tissue of the mucous membrane contains fasciculi of connective tissue, and a considerable quantity of coiled elastic fibres of various size united into plexuses. The part situated immediately beneath the epithelium, is much closer

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* E. Klein, *Uber das Epithel des Weichen Gaumes*, etc., "On the Epithelium of the Soft Palate," etc.; *Wiener Sitzungsberichte der k. k. Akademie der Wissenschaft. zu Wien*, Jänuar heft, 1868.

in texture than that which is deeper, and forms the submucous tissue in which the glands and muscles are found. The fasciculi of connective tissue found in the velum palati and uvula may be considered to run in three directions; the first of these, for the most part lying externally, run horizontally and from side to side; the second longitudinally; and these two sets form the felt of the mucosa; lastly, there is a third set, which, emanating from the first two, runs from the mucosa in an obliquely divergent manner into the deeper parts, in order to enter the mucosa of the opposite side. These last-mentioned fibres form, by their decussation, the loose network of the submucous tissue of the soft palate and uvula, which, as usual, contains a variable quantity of fine elastic fibres, small lymph corpuscles, and large connective tissue corpuscles, with numerous vessels and nerves. In the soft palate and uvula of the adult there project from the surface of the mucous membrane into the epithelial layer conical or cylindrical papillæ with rounded extremities. These papillæ are much larger and more numerous on the uvula than on the soft palate. (In one transverse section of the uvula of an adult I counted 130 in a single plane.)

In the velum palati of the new-born infant the relations of these parts are somewhat different. In such I find no papillæ on the upper surface, but the vessels advance as far as the epithelium, and there loop back, or course for some distance immediately beneath the epithelium. On the inferior surface again we find similarly looped vessels forming broad and flat arcades, especially in longitudinal sections, immediately subjacent to the deeper surface of the epithelium, or a bloodvessel with a little mucous tissue may project into the inferior layer of the epithelial cells. These appearances may be remarkably well seen at the borders of the folds. Two or three branches may there be seen to be given off from a larger vessel, and, accompanied by a little fibrous tissue, to penetrate between the epithelial cells. At the most prominent portion of the folds two or three pointed papillæ appear of equal breadth but variable length. The mucous membrane of the velum palati is extraordinarily rich in vessels. Just beneath the epithelium, as well as in the deeper layers of the

mucosa, besides numerous extremely thin-walled bloodvessels, there are numerous lymph channels, both in the form of larger lymphatic lacunæ and of lymphatic vessels. The larger nerve trunks lying externally to the first rows of glands, the number of which is much more considerable at the anterior than at the posterior surface, give off fine branches, which run both internally into the submucous tissue as well as externally into the mucosa, where they may be followed in the former instance between the glands and the muscles, in the latter as far as the epithelium.

The thickness of the mucosa is variable, and depends on the size and number of the glands. In general the thickness of the mucous membrane increases from the commencement of the hard palate towards the point of the uvula, and it is always somewhat thicker on the upper surface than on the lower.

The acinous mucous glands of the soft palate are situated, as has been noted above, in the submucous tissue. Their size varies, and the largest are found in the uvula. Szontagh* counted one hundred of them on the anterior surface of the soft palate, forty on the posterior surface, and twelve on the uvula. In the last-named situation they become larger, and form in its upper half, or basis, a central layer, which, however, is somewhat nearer to the anterior surface than to the posterior, and is sometimes invested by the fasciculi of the azygos uvulæ, and at others is intercalated between the two muscles.

The excretory ducts vary in their width, in the nature of their coats, and in their direction. At the posterior surface of the uvula in adults we find excretory ducts which become wider near their orifice; but the opposite obtains in the ducts opening on the upper and lower surfaces of the soft palate. The direction pursued by the excretory ducts is very rarely rectilinear; the greater number, after they have received all their tributary branches, run from the deepest part of the mucosa perpendicularly towards the epithelium, then turn off at an angle, and course obliquely towards the free surface of the epithelium. They are for the most part lined with a simple cylindrical epithelium; in other instances, but less fre-

* *Loc. cit.*

quently, beneath the cylindrical cells a second layer of small round cells is found, and at the posterior surface of the soft

Fig. 104.

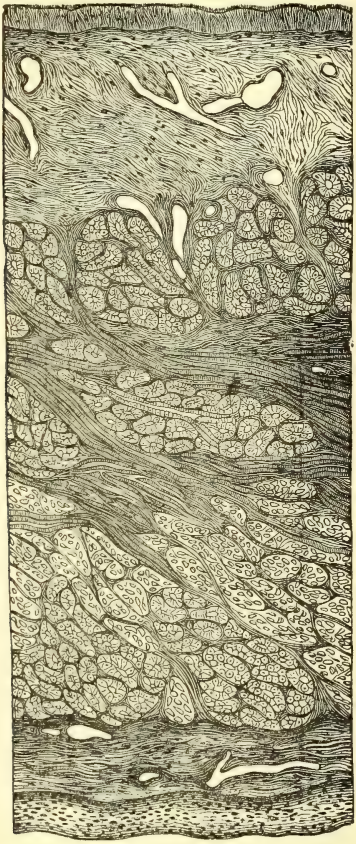

Fig. 104. Longitudinal section of the soft palate of a Child. *a a*, ciliated epithelium; *b b*, mucous membrane of the upper surface; *c*, glands; *d d*, muscular fibres of the thyreo-palatinus; *e e*, muscular fibres of the levator palati; *f*, mucous membrane of the lower surface; *g*, epithelium of the lower surface.

palate the excretory ducts of a few glands exhibit, even in the adult, for a short distance from the epithelial surface, a lining of

ciliated cylindrical cells.* The laminated pavement epithelium of the surface may in some cases be followed for a short distance as a lining to the excretory ducts of the glands.

The course and arrangement of the muscles in the soft palate are highly complicated. The only true longitudinal muscle contained in it is the azygos uvulæ, or palato-staphylinus, a double muscle, the two portions of which arise at the fibrous border of the hard palate, and are situated on either side of the median line. In the anterior part of the soft palate the two portions are distant from each other about their own diameter,† but near the base of the uvula they are in close proximity. They do not quite extend to the apex, but terminate at about the end of the second third, the fasciculi becoming fan-shaped anteriorly, and expanding to the greatest extent at the sides, consequently corresponding in their course, and terminating in the same mode as has been described in speaking of the muscles of the lips. In their passage through the soft palate, several small fasciculi are given off from the principal mass, which, traversing the lobules of the glands, and surrounding them, rejoin it, or dip into the mucous membrane, especially at its anterior surface, and terminate in the mode described.

The Musculus thyreo-pharyngo-palatinus‡ constitutes the chief muscular mass of the soft palate. It is divisible, according to Luschka, into a thyreo-palatine and a pharyngo-palatine portion. The upper extremity of the former lies partly in front of and partly behind the Levatores, decussating with them to some extent. The greater number of the fibres of the pars thyreo-palatina lie in front of the Levatores, and form a curved flattened muscle, with a maximum breadth of nine millimeters which is situated nearer to the hard palate than the arch formed by the junction of the two Levatores by about the breadth of this arch. The convex border of this portion is continuous with the fibrous border of the hard palate or aponeurosis of the tensor veli palati, whilst its concave border

* E. Klein, *loc. cit.*

† Szontagh, *loc. cit.*

‡ Luschka, *Der Musculus pharyngo-palatinus des Menschen,* Virchow's *Archiv,* Band xlii., p. 480.

is turned towards the similar concave border of the arch formed by the Levatores.

The other fibres of the upper extremity of this pars thyreo-palatina, situated behind the Levatores, form in the adult several loosely connected fasciculi, much interrupted by fat cells, which, becoming more and more delicate towards the free border of the soft palate, course partly in front of the azygos uvulæ between the glands of the anterior surface, and partly over or behind it between the glands of the posterior surface, either ending here or extending to the mucous membrane. The thyreo-palatine portion of the muscle just described receives reinforcing fibres from the Levatores;* and a fasciculus is constantly given off laterally from these where they unite to form an arch, which, subdividing, runs in front of the azygos to the opposite side, and there joins the innermost bundles of the pars thyreo-palatina. The whole of these fibres run outwards and downwards, descending with the arcus pharyngo-palatinus, and are partly inserted in the upper angle of the thyroid cartilage, and are partly united with the pars pharyngo-palatinus, forming the posterior wall of the pharynx. The pars pharyngo-palatina arises near the arcuate extremity of the pars thyreo-palatina, and the two unite together in the arcus pharyngo-palatinus, and pass to the posterior wall of the pharynx. Besides what has been already stated respecting the Levatores veli palati, it still remains to be observed that the arcuate junction of these two muscles is situated in front of the azygos uvulæ, and in the anterior half of the soft palate.

Finally, there is a small muscular fasciculus which arises from the transverse fibres of the tongue, and runs in the anterior arcus glosso-palatinus towards the base of the uvula, where it is partly lost in the mucous membrane of its anterior surface, and partly unites with the ultimate bundles of the thyreo-palatinus.

The several fasciculi of the palatal muscles, like those of the tongue and lips, form a delicate plexus. A considerable quantity of adipose tissue generally enters into the structure of the palate in adults, being chiefly found between the fasciculi

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* Luschka, *loc. cit.*, p. 483.

of the thyreo-palatinus and the levator palati. It also constantly occurs between the first layer of glands of the upper surface, and is to be met with, in larger or smaller quantity, in various parts of the mucous membrane.

The muscular folds of the mucous membrane which extend as the arcus glosso-palatinus and pharyngo-palatinus, from the soft palate to the root of the tongue and pharyngeal wall, exhibit no peculiarity of structure differing from that of the mucous membrane of the soft palate; the epithelium, papillæ, and muco-membranous tissue being in all essential respects similar. Elastic tissue, forming plexuses, is usually abundant in the mucous membrane of these folds. The lowermost glands diminish in number and size in adults, present the same dimensions as those of the uvula, and are united into a layer, the continuity of which is interrupted by a sparing amount of loose connective tissue containing fat cells surrounding the lobules and acini, and here and there by small muscular fasciculi. The tissue of the mucous membrane is frequently infiltrated at the free border of the folds with a greater or less number of lymph corpuscles. These infiltrated portions, in which may be recognised, besides numerous bloodvessels, a delicate cellular network with decussating fibres of connective tissue, are never sharply defined, but pass gradually into the adjoining tissue.

Between the palatine arches the lateral walls of this part of the oral cavity, known as the Isthmus faucium, present a depression; from the bottom projects a swelling—the tonsil, which is sometimes so small in newly born children as to be scarcely perceptible on inspection of the oral cavity from before, and is sometimes so large that the two organs materially contract the dimensions of the isthmus. Their surface is lobulated by fissures of various depths and complexity. The whole organ is to be regarded as a thickened portion of the mucous membrane, presenting a lobulated surface, the proper membrana mucosa of which constitutes a kind of conglobate gland substance (Henle), consisting partly of fibrous, and partly of adenoid tissue, in the meshes of which numerous lymph corpuscles are contained. The epithelium is here tesselated and laminated; papillæ can scarcely be said to be present. Beneath the epithelium is a close plexus of vessels, and the

infiltrated mucosa is divided into portions resembling Peyer's patches by means of connective tissue cords proceeding from the submucous tissue. Acinous glands are distributed in the submucous tissue, and they are in contact externally with the muscular tissue of the pharynx.

The Tongue.

That surface of the tongue in Man which is directed towards the palate—dorsum of the tongue—presents different characters from the lower surface; for in the former the papillary elevations of the mucosa covered with tesselated epithelium project to a considerable extent, and confer upon it its peculiar furred appearance; whilst on the lower surface the papillæ of the mucous membrane do not in general project more than to half the thickness of the epithelium. The surface of the descending portion of the tongue in the newly born child, again, presents different features from that of the adult; in the former, the surface of the mucous membrane appears tumified, the swellings being divided by elongated fissures; in adults, on the other hand, it is beset in many places with numerous smaller and larger lenticular elevations, which sometimes possess a small opening. The mucous membrane on the lower surface of the tongue, when in the contracted condition, exhibits numerous fine parallel folds like those which, under all circumstances, are to be found upon the sides, posterior to the level of the foramen cæcum.

The papillæ freely projecting from the surface of the tongue are termed, in accordance with their form, (*a*) filiform—papillæ filiformes; (*b*) club shaped—papillæ fungiformes; and (*c*) circumvallate—papillæ circumvallatæ. The so-called filiform papillæ are conical, and in the newly born are simple and rounded at their extremity; whilst in adults they are compound, and frequently prolonged into hair-like processes. The clavate or fungiform papillæ are thinner at the basis than at the apex, which appears expanded into a club-like body, and in adults is provided with secondary apices.

The circumvallate papillæ, lastly, are the largest, and are only distinguishable from the fungiform by the wall of mucous

membrane which surrounds them; and this is so indistinct in most instances in newly born children, that no difference can be discerned between them and the clavate papillæ. As regards the distribution of these various papillæ on the tongue of Man, the papillæ filiformes are spread in nearly equal numbers over the whole dorsal surface of the horizontal part, and on the edges.

The fungiform papillæ are found on the anterior portion of the dorsal surface, and chiefly near the tip and edges; towards the median line of the posterior portion they become more sparing and small, and altogether cease at the root of the tongue. It only happens in some few cases that filiform papillæ are found in the latter region, and still more rarely the fungiform.

The papillæ circumvallatæ are most limited in number; they are placed on each half of the tongue at the junction of the dorsum and the root, and are so arranged that they form a V, the point of which is at the foramen cæcum.

The epithelium both of the upper and lower surfaces is tesselated and laminar; in the filiform papillæ of the tongue of adults the pavement cells are arranged in an imbricated manner, and are provided with longer or shorter processes which project freely beyond the papillæ; the most superficial flattened and horny cells sometimes form solid hairs or fibres, freely projecting beyond the secondary papillæ. The epithelium of the tongue is elsewhere similarly formed to that of other parts of the oral cavity.

The mucosa is thinner in the fore or horizontal part of the tongue in Man, and is, at the same time, much more intimately connected with the subjacent muscles than in the descending portion, where, on account of the abundant loose submucous tissue with numerous glands imbedded in it, it is easily movable; its elements are the same as those of the mucosa in other parts of the oral cavity; fibres of connective tissue being united into fasciculi, and forming a close network that is connected with the deeper tissues by strong trabeculæ.

The so-called septum cartilagineum of the human tongue, which, arising from the hyoid bone, appears as a dense vertical median plate situated between the Genio-glossi, and extending through the whole length of the organ, gradually diminishing

in height towards the apex, is, as Kölliker* has shown, incorrectly named, since it is composed exclusively of connective tissue.

The mucous glands of the human tongue occupy the sides and root of the organ; amongst the former are those described by Blandin† and Nuhn.‡

Nuhn found at the apex of the tongue of Man, lying beneath the mucous membrane and a layer of longitudinal muscular fibres formed by the styloglossus and longitudinalis inferior, a symmetrically placed pair of glands, from seven to ten lines long, three to four and a half lines broad, and one and a half to two and a half lines thick, opening by five orifices on the lower surface of the apex. N. Ward§ once found at this point an azygous gland, placed transversely, one-third of an inch broad, and one-eighth of an inch long, with three fine excretory ducts.

On the lateral border of the tongue, near the styloglossus, there may also be found a median and a more constant posterior group of glands, which either open close to the edge of the tongue, or more rarely in the floor of the mouth.

The glands at the root of the tongue form, beneath the posterior non-papillated portion of the mucous membrane, a continuous layer of six millimeters in thickness, partly imbedded in the musculature.‖ The excretory ducts of these glands open, in the newly born infant, in the hollows between the ridges; but in adults, in some instances, in the so-called crypts of the root of the tongue, which, according to Salter,¶ constitute reservoirs for the acinous glands. Many of these reservoirs extend, according to this observer, as elongated, sometimes branched, passages for one-half to three-fourths of

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* *Beiträge zur Anatomie der Mundhöhle, Würzburger Verhandlung*, Band ii., p. 169.

† *Anat. topograph.* Paris, 1834, p. 175.

‡ A. Nuhn, *Ueber eine bisjetzt noch nicht näher beschriebene Drüse im Innern der Zungenspitze*, "On a hitherto undescribed gland in the apex of the Tongue." Mannheim, 1845.

§ N. Ward, *loc. cit.*

‖ Henle, *Splanchnologie*, p. 141.

¶ Todd's *Cyclopædia*, Vol. iv., p. 1140.

an inch beneath the surface, and receive at various points the excretory ducts of the mucous glands.

In the wall of these so-called crypts of the root of the tongue, according to Kölliker,* closed follicles filled with lymph corpuscles are imbedded. He describes each of these saccular glands which receive at their base the excretory duct of an acinous mucous gland, as consisting of a thick-walled capsule, surrounded externally by a fibrous sheath, and lined internally by a prolongation of the oral epithelium. Between these two, and contained in a delicate, fibrous, vascular, and at the free surface papillated matrix, lie a number of closed lymph follicles of 0·1 to 0·25 of a millimeter in diameter, forming a continuous, but for the most part single layer.

Huxley† has corroborated generally the correctness of the description given by Kölliker of the glands at the root of the tongue, but finds the crypts of the mucous membrane surrounded, not by closed follicles, but by an indifferent cell containing tissue, traversed by capillaries. Sappey‡ has only observed the acinous glands opening into the crypts, but not the closed follicles; and whilst Sachs§ is very doubtful of the presence of follicles in the wall of the sacculi, Franz Gauster and Eckhard‖ give their support in all respects to the statements of Kölliker.

Gerlach¶ states that he has found follicles in the wall of some only of the lingual sacculi.

The conclusions at which Arthur Böttcher** arrived, have quite a different tenor. He found

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* *Beiträge zur Anatomie der Mundhohle, Würzburger Verhandlung,* Band ii., p. 177.

† Huxley, "On the Ultimate Structure and Relations of the Malpighian of the Spleen and Tonsillar Follicles," *Microscopical Journal,* Vol. ii., p. 74.

‡ *Recherches sur la structure des Amygdales et des glands situées sur la base de la Langue, Comptes rendus,* 1855, No. 22.

§ *Observationes de Linguæ structura penitiori,* Vratislav, 1856; and *Zur Anatomie der Zungenbalgdrüsen und Mandeln,* Reichert and Du Bois Reymond's *Archiv f. Anat. u. Physiologie,* 1859, p. 196.

‖ G. Eckhard, *Zur Anatomie der Zungenbalgdrüsen und Tonsillen,* Virchow's *Archiv,* Band xvii., p. 171.

¶ *Handbuch der Gewebelehre,* 1854, p. 297.

** Arthur Böttcher, *Einiges zur Verstandigung in Betreff der Balgdrüsen*

1. That there are some tongues which do not possess any saccular glands.

2. That the occurrence of exceedingly well-developed sacculi is coincident with disease of the mucous membrane.

3. That between these two there are intermediate conditions in which it is often difficult to decide whether a slight elevation of the mucous membrane of the tongue, with a duct in the centre, is to be regarded as a saccular gland or not.

He is therefore of opinion, (1) That in the healthy tongue there are no saccular glands; (2) That these are swellings caused by disease in the immediate vicinity of the ducts of the mucous glands; and that consequently the follicles in their interior are also neoplastic pathological formations.

I am able to corroborate the statement made by Böttcher, that there are some tongues in which no follicular glands are present, and to add that in such cases the mucous membrane in different parts and to a variable extent of the root of the tongue, as well as the loose tissue of the soft palate of the uvula, and of the upper pharyngeal wall, is infiltrated with lymph corpuscles. These infiltrated parts are destitute of a distinct limiting membrane or capsule.

The flat lenticular elevations of the root of the tongue usually present in adults are merely portions of the mucous membrane in which conglobate glandular substance is imbedded. The central orifice they exhibit is the entrance to a little pit which, like the projections themselves, is lined with tesselated epithelium. At the root of the tongue in the newly born infant the mucous membrane presents no saccular glands. It only exhibits here and there in the above-described ridges, between which the mucous glands open, isolated small or larger groups of cellular elements. These are also present at the bases of the papilla of this part, and in the tissue of the mucosa.

The foramen cæcum, situated in the descending portion of the tongue, though not always, and indeed, according to Boch-

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an der Zungenwurzel, "A few Observations explanatory of the nature of the follicular glands at the root of the Tongue;" Virchow's *Archiv,* Band xviii., pp. 190—220.

dalek, junior,* only thirteen times in fifty cases, is continued, by its fundus or posterior wall, which presents a larger or smaller opening directed backwards in the muscular substance of the tongue, into a simple or branched cæcal ductus excretorius linguæ, so called because it constitutes the excretory duct common to a large number of mucous glands.

The epithelium of the foramen cæcum is of the ordinary transitional variety; that of its excretory duct, as well as of its cæcal appendix, is cylindrical and ciliated. The foramen cæcum, according to Bochdalek, is *not* formed by an increase in depth of the most posterior papilla circumvallata.

In regard to the lymphatics of the tongue, Sappey† has shown that delicate vessels proceeding from the close lymphatic plexuses of the mucous membrane penetrate into the papillæ, and form a superficial network. According to Teichmann,‡ the lymphatics are confined to the mucosa and submucosa, and form a plexus with coarse deeply situated and more delicate superficial vessels.

In the papillæ filliformes, a few vessels with cæcal terminations, proceeding from a capillary ring, enter some of the papillæ. At the base of the papillæ fungiformes, again, a circular plexus of vessels is found, and lymph capillaries are present both in the circumvallate papillæ and in the adjoining tissue.

The muscular fibres of the tongue are vertical, transverse,§ and longitudinal, the first set belonging to the musculus perpendicularis at the apex, to the genio-glossus in the middle, and to the lingualis and hyoglossus at the sides. Between these vertically arranged fasciculi run those of the transversus linguæ, and in part also of the styloglossus, directed in each half of the tongue from the septum towards the lateral surface.

Finally, in immediate proximity with the mucous membrane,

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* Bochdalek, junior, *Ueber das Foramen Cæcum der Zunge, Oesterreichische Zeitschrift für Heilkunde*, Nos. 36—46.

† Sappey, *Comptes rendus*, 1847, p. 26.

‡ Teichmann, *Das Saugadersystem vom anatomische Standpuncte.* Leipz'g, 1861, p. 113.

§ Salter, Todd's *Cyclopædia*, p. 1125; and Kölliker, *loc. cit.*, p. 169.

are the longitudinal fibres belonging to the longitudinalis superior and inferior, as well as the greater part of the styloglossus. As a general rule, the vertically ascending as well as the transverse fasciculi penetrate into the mucous membrane through those of the longitudinal muscles, becoming, at the same time, considerably thinner. They also decussate with each other, both before they reach the longitudinal fibres, and after they have emerged from them, when they enter into the mucous membrane.

The longitudinal muscles give off several small fasciculi and fibres to the mucous membrane.

In the *cat* the filiform papillæ situated about the middle of the dorsal surface are best developed ; they are here also most numerous, and each is prolonged into one or several recurved horny points. Towards the lateral surfaces of the horizontal portion they rapidly diminish in size, and at the edge cease to be distinguishable to the naked eye ; so that here the papillæ fungiformes, which elsewhere on the dorsal surface are situated at tolerably regular distances between the filiform, are seen to project as whitish beads, at considerable distances apart. It is only at the most anterior part of the tongue that the filiform papillæ are distributed over its edges, and extend for a short distance on the inferior surface. At the border of that part of the tongue which corresponds to the junction of the horizontal with the descending portion is found a longitudinal series, from ten to fifteen in number, of cylindrical filiform papillæ, capitate at their extremities, of which the centre ones are longer (three millimeters) than either the anterior or posterior (one millimeter). Towards the root of the tongue the filiform papillæ decrease in number and size, and appear in the form of isolated very broad projections, terminating in a short, soft, recurved point.

In *rabbits*, on the dorsal surface of the tongue, as far back as the descending portion, and on the upper part of this, only closely approximated papillæ filiformes are found, which are absent at the edges, except where the horizontal is continuous with the descending portion. Over the well-known whitish elongated oval elevation of the tongue of the rabbit the papillæ are somewhat larger than on other parts of the dorsal surface. Behind this elevation the mucous membrane presents a smooth surface as far as two small projections constantly situated on either side of the median line, and apparently belonging to the papillæ circumvallatæ.

At the junction of the horizontal with the descending portions on the border of each side of the tongue is found a slightly depressed semi-circular spot, the periphery of which touches the posterior part of the oval prominence. The surface is not smooth, but covered with delicate, parallel, vertically arranged folds, on a few of which a filiform papilla may be here and there discerned.

This portion, as well as the above-mentioned minute folds at the border of the tongue in man, and the group of papillæ found at the junction of the horizontal and descending portions of the tongue in the cat, correspond to the peculiar organ described by Weber,* and especially by J. C. Mayer,† in many mammals under the term of papilla lingualis foliata.

The papillæ of the tongue of the rabbit appear considerably shorter than those of man, and this is due to the absence of depressions in the epithelium between them.

The thickness of the epithelium diminishes from before backwards, and also towards the sides; yet, posterior to the oval prominence, is as thick as at the apex of the tongue.

The structure of the mucosa does not differ from that of man. Its thickness also diminishes from the tip towards the oval prominence. At the root of the tongue the fasciculi of muscular fibres situated beneath the mucosa form a rectangular network, in the loculi of which are contained the lobules of the acinous glands. The excretory ducts of these glands penetrate the mucosa in a vertical direction to reach the surface. Numerous small masses of lymph corpuscles are to be met with around and between the lobules of the glands. In the depressed semi-circular portion of the border of the tongue the laminated pavement epithelium is much more attenuated on the margin of the folds than on their sides. The depths of the folds amount to 0·45 of a millimeter, and the mucous membrane projects into them in the form of an acute angle.

The excretory ducts of large acinous glands open into the grooves intermediate to the folds, the relation of which to the muscular fasciculi is similar to that already described in the case of the glands at the root of the tongue. A considerable number of nerves,

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* Weber, in Hildebrandt's *Lehrbuch der Anatomie*, Band., iv, 4. Aufl. p. 150.

† J. C. Mayer, *Untersuchungen aus dem Gebiete der Anatomie*, etc. Bonn, 1842, p. 25.

the fibres of which are all medullated, are contained in the mucous membrane at the bottom of the folds.

The transversus linguæ exhibits a looser arrangement, as it extends from the middle line of the upper surface to the lower, in that its fasciculi describe arches, which diminish in length towards the border of the tongue.

In the tongue of the *frog* the papillæ filiformes are distributed over the whole dorsal surface ; towards the posterior cornua they diminish in number and size, and cease at some distance from their apices. There is also a lateral zone of the dorsum extending along the whole length of the tongue, and from two to three millimeters in breadth, which is destitute of papillæ. The fungiform papillæ are similarly arranged. The two forms are most numerous and largest at the anterior part of the dorsal surface. The papillæ filiformes are thin and long, but towards the cornua of the tongue they are somewhat broader. The epithelium, throughout the entire cavity of the mouth, consists of a laminated and ciliated columnar epithelium, with the exception of the apices of the papillæ, where the most superficial cells are short cylinders, destitute of cilia.* Neither Hartmann nor Hoyer† were able to recognise the continuity of the processes of the columnar epithelium covering the papillæ with the connective tissue corpuscles, as described by Billroth‡ and Axel Key.

On the lower surface of the tongue the epithelium is formed by two or three layers of pavement cells, the most superficial in some parts bearing cilia.

A nerve trunk, composed of dark-edged fibres, occupies the centre of the fungiform papillæ, whilst at their periphery is a capillary plexus opening into a central vessel ; situated peripherically also are muscular fibres which frequently undergo division in their passage upwards. Moreover, transversely situated muscular fibres extend into the fungiform,§ and into some of the filiform papillæ, though they can seldom be followed to the apex.

The glands of the tongue of the frog are pretty equably distributed over the whole of the dorsal surface ; anteriorly they are more closely assimilated to the type of the acinous glands than posteriorly. The

* Leydig, *Histologie*, 1857, p. 307. Axel Key, Reichert and Du Bois' *Archiv*, 1861, p. 228. Hartmann, *idem*, 1863, p. 634.

† Hoyer, *Mikroskopische Untersuchungen über die Zunge des Frosches*, Reichert and Du Bois' *Archiv*, 1859, p. 501.

‡ *Ueber das Epithel der Froschzunge*, Müller's *Archiv*, 1859, p. 159.

§ Waller, *Philosophical Transactions*, 1847.

excretory ducts, especially of the anterior part, support laterally and terminate at their extremities in hemispherical enlargements, or they pursue a closely coiled course, and are then more deeply imbedded between the muscles. As a general rule, they are only surrounded by muscular tissue at their fundus.

The glands are lined by columnar epithelium, the cells of which become shorter in the deeper acini. A few of the cylindrical cells near the orifice sometimes support cilia.

At the posterior part of the dorsal surface, and especially on the posterior processes of the tongue, the glands constitute longer o shorter tubes, which are for the most part inflated or irregularly prominent at their fundus. Here also their fundus is imbedded amongst the muscles which run up from the deeper parts and accompany the gland ducts for a variable distance towards the surface. The cylindrical epithelium with which they are lined behaves in the same manner as that of the glands of the anterior portion.

Division of muscular fibres occurs, to a considerable extent, in the frog, as well as in the newt, calf, bat, sheep, goat, and cat, and also in man. In man, Rippmann* saw simple and individual muscular fibres run out into two, three, or even four moderately long branches.

According to Remak,† microscopic ganglia are situated on the branches of the glosso-pharyngeus, and of the ramus lingualis. And he believes the same relations to subsist between the glands and ganglia of the tongue, as between the submaxillary gland and the ganglion submaxillare.

B. PHARYNX.

With the pharynx the digestive tract begins to be independent, and at its lower part assumes a tubular character, whilst, at the same time, it is distinctly differentiated into mucous membrane, muscular layers, and an external investing fibrous membrane.

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* Th. Rippmann, *Ueber das Vorkommen von Theilungen der Muskelfasern in der Zunge der Wirbelthiere und des Menschen,* "On the occurrence of Division in the muscular fibres of Vertebrata and of Man;" Henle and Pfeuffer's *Zeitschrift,* 3. Reihe, Band xiv., p. 200.

† *Ueber die Ganglien der Zunge bei Saügethieren und Menschen,* "On the Ganglia of the Tongue in Mammals and in Man;" Müller's *Archiv,* 1852, Heft 1, p. 58.

The *epithelium* of the mucous membrane in the portions immediately adjoining the nasal cavity is laminar and tesselated. This form of epithelium extends, according to Schmidt,* to the posterior edge of the so-called pharyngeal tonsils, but their anterior portion, as far as the orifice of the Eustachian tube, possesses a columnar and ciliated epithelium. The distribution of the latter in the regions in question is most extensive in the new-born child, extending here over the whole of the upper portion of the pharynx, known as the cavum pharyngo-nasale. In the adult, on the other hand, it never extends over more than the upper third. Both the epithelium and mucosa are similar in their characters to the same structures of the soft palate.

The free surface† of the nasal region of the pharynx, occupying the interspace between the Eustachian tubes, and extending from the posterior portion of the roof of the nasal cavity to the anterior border of the foramen magnum, exhibits in most instances a delicate longitudinal striation, with laminæ or folds separated by deep fissures, which to some extent become united, giving rise to a plexiform pattern; and frequently the surface is covered with low elevations, traversed by a variable number of short, often irregularly running fissures. These folds exhibit numerous whitish, poppy-seed-like enlargements, with a considerable number of roundish pores, which are partly recognisable as the entrance to little isolated pits of the mucous membrane, but are chiefly the orifices of acinous glands.

A larger opening, though not constantly present, is found in the lower half of the median line of the roof of the pharyngeal cavity. It constitutes the entrance to the process of the pharyngeal arch which ascends to the body of the occipital bone, and is usually surrounded by acinous glands, but sometimes also by a muscle. It has been named by J. C. Meyer the Bursa pharyngea.

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* Schmidt, *loc. cit.*

† Luschka, *Das adenoide Gewebe der Pars Nasalis des menschlichen Schlundkoppes*, "The adenoid tissue of the nasal portion of the Pharynx of Man;" *Archiv für wissenschaftliche Anatomie*, v. Max Schultze, Band iv., Heft 1, Seite 5—9.

The thickenings or folds of the mucous membrane of the pharyngeal arch, as well as the walls of the bursa above described, consist of a loose vascular tissue infiltrated with lymph corpuscles, exhibiting in parts the same structure as that which we have seen in numerous portions of the soft palate. At those points where the poppy-seed-like bodies are observed, the mucous membrane presents, over a larger or smaller surface, an adenoid structure closely packed with lymph corpuscles. These infiltrated spots, although constructed on the same plan as the lymph follicles, have, like the similar spots at the root of the tongue, where they are more sparing in number and smaller, no distinct investing membrane.

Luschka* has denominated this part, first described by Lacauchie,† the Tonsilla Pharyngea, and he agrees with Kölliker in regarding it as an aggregate of lymphatic glands. Henle,‡ on the other hand, holds it to be conglobate gland substance. It forms a mass of about eight millimeters in thickness, which extends to between the orifices of the Eustachian tubes, from the posterior extremity of the roof of the nasal cavity, with an average length of three centimeters.

The glandular tissue is in great part divided into laminæ with deep intervening fissures, or is arranged in the form of round sacculi, the walls of which, having an average diameter of one millimeter, are lined by ciliated epithelium and a continuation of mucous membrane, communicating with the exterior by a very narrow orifice. The tissue of the mucous membrane covering the arch of the pharynx is differentiated from that of the lower part by the circumstance that it exhibits over surfaces of considerable extent the characters of lymphatic glandular tissue.

The mucous membrane of the middle third of the pharynx, though more sparingly than in the upper portion, is also infiltrated with numerous cellular elements, which are either irregularly distributed through its substance or lie collected into dense masses in a vascular stroma.

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* Luschka, *Anatomie des Menschen.* Tubingen, 1862, Band i., Abschnitt 1.

† *Traité d'Hydrotomie*, 1853, Tab. ii., fig. 10.

‡ Henle, *Splanchnologie*, p. 146.

In infants the mucous membrane exhibits a great number of oblong nucleated elements, the extremities of which are drawn out into fine pointed processes which penetrate between the fibres of the tissue. This peculiarity may be observed in several parts of the above-described portions of mucous membrane, and appears therefore to be characteristic of an embryonic condition of the tissue. Wherever the epithelium is laminar and tesselated, numerous papillæ, narrow at their base, and clavate at their free extremity, project from the surface of the mucosa, and penetrate the epithelial layers to about half their depth; but where the epithelium of the roof of the pharynx is laminated, and composed of cylinders supporting cilia, the papillæ are altogether absent.

The large *vessels* form a plexus beneath the epithelium, giving off finer branches, which either pursue a longer or a shorter course parallel to the surface, or form loops immediately beneath the epithelium. In the middle third of the membrane in adults, and especially in the lower parts, are numerous papillæ arranged with tolerable regularity. In the upper parts they are in some parts imperfectly developed, and here and there are altogether absent. In the lower third the papillæ are both constantly present and numerous.

In the infant the *papillæ* are only feebly developed, either in the form of slight sinuosities of the mucous membrane projecting into the epithelial layers, or as sharply pointed papillary elevations composed of connective tissue and blood-vessels, especially over those parts of the membrane presenting striæ or folds, which penetrate to a variable extent into the epithelium.

As it approximates the muscular tissue the structure of the mucous membrane becomes looser, forming the *submucous tissue;* and the fasciculi, which constitute a plexus with meshes of various sizes, are arranged in the upper and middle third in a horizontal direction, or run obliquely backwards and outwards between the fasciculi of the muscular layer to the outer fibrous layer, as well as in the opposite direction from this inwards and downwards, some few fasciculi penetrating between the muscles into the submucosa, in which they are gradually lost as they descend. In the lower third, the fasciculi of the

mucosa pursue various directions, but those of the submucosa are chiefly directed downwards.

The acinous *glands* of the pharynx, especially in the middle and lower parts of the upper third, form groups, the excretory ducts of which open with wide orifices. The individual glands are oval, with their long diameter parallel to the long axis of the tube. In the lower third they diminish considerably in number, so that at the upper part of this they only occur in an isolated condition, whilst below they are but rarely met with.

The depth of the mucosa varies with the thickness of the glandular layer, but diminishes gradually in the lower third towards the œsophagus. The larger *nerve trunks* lie in the submucous tissue, and run for the most part in a longitudinal direction, whilst their branches form a deep and a superficial plexus, in the latter of which Remak* and Billroth observed the presence of microscopical ganglia.

The *lymphatics* of the pharynx are numerous, and, according to Teichmann,† are directly continuous with those of the nose, oral cavity, trachea, and œsophagus.

The *outer fibrous layer* of the posterior wall of the pharynx, attached above to the base of the skull, extending downwards, and containing a median tendinous fasciculus which arises from the tuberculum pharyngeum, consists chiefly of strong parallel bundles of fibrous tissue, with a variable amount of finer and broader elastic fibres. These for the most part descend obliquely with the fasciculi accompanying the nerves and bloodvessels, and with others derived from the submucous layer form sheaths for the pharyngeal muscles, and give off the secondary septa for the smaller muscular fasciculi.

The *muscular layers* of the posterior, and partly also of the lateral, walls of the pharynx are so arranged as to form an essentially circular external and an internal longitudinal layer. The former is composed of the Constrictores pharyngis, the

* Remak, *Ueber peripherische Ganglien an den Nerven des Nahrungsrohres*, Müller's *Archiv*, 1856, p. 189; "On the Peripheric Ganglia of the Nerves of the Alimentary Canal." A contest respecting priority with Meissner, in which it was shown that Remak had previously, in 1840, found ganglia in the tongue and on the pharyngeal branches of the Glosso-pharyngeus.

† *Loc. cit.*

latter is formed by the Stylo-pharyngeus and Thyreo-pharyngo-palatinus,* from the pharyngo-palatine portion of which a few fasciculi are given off which pursue a horizontal direction, uniting on the posterior wall of the pharynx with those of the opposite side to form a series of arches with their convexity directed downwards.

A few small fasciculi are also given off from the most internal muscular bundles, especially at the lower part of the pharynx, which, running downwards, penetrate the mucous membrane obliquely, and terminate in it.

The mucous membrane of the pharynx, which is connected by means of short connective tissue fibres with the posterior surface of the larynx, presents the same structure as that of the lower third of the posterior wall.

The glands are here also elongated, and form a continuous layer above, whilst they diminish in number below to such an extent that it is rare to meet with one on the anterior wall of the œsophagus. The excretory ducts of these glands are directed obliquely downwards, so that on examining transverse sections, numerous ducts may be found without any of the glands being present. They become somewhat wider beneath the epithelium, and here possess, lining their interior, a series of well-marked cylindrical cells, subjacent to which are two or three rows of smaller spheroidal cells with comparatively large nuclei.

Adipose tissue is found in considerable quantity in adults, occupying the interspaces of the muscular fasciculi and of the glands of the mucous membrane situated on the posterior surface of the larynx.

c. Œsophagus.

Commencing at the level of the lower border of the cricoid cartilage, the alimentary canal extends, in the form of a completely closed tube, to the foramen œsophageum of the diaphragm. In the undistended condition the mucous membrane forms parallel longitudinal folds, and is attached to the subjacent muscular coat by loose connective tissue.

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* Luschka, Virchow's *Archiv*, Band xlii., p. 485.

In Man it is lined by laminated pavement epithelium, the cells of which, both in their form and arrangement, resemble those of the lower part of the pharynx.

The membrana mucosa is situated between the muscular layer of the mucous membrane which commences with the œsophagus, and the epithelium, and it is separated by this muscular layer from the thicker layer of the submucous tissue which occupies the interval between the muscularis mucosæ and the muscularis externa.

In newly born children* the mucosa exhibits in many parts the structure of adenoid tissue. In others, again, numerous bloodvessels are found, running for the most part in a longitudinal direction beneath the epithelium, and accompanied by a sparing amount of connective tissue derived from the external portion of the mucous membrane.

In adults the longitudinal fasciculi of connective tissue derived from the submucosa run inwards between the fasciculi of muscularis mucosæ, and then either pursue a sinuous course parallel to each other, or form plexuses. A great number of cellular structures are constantly found amongst them.

The surface of the mucous membrane is beset in adults with a large number of conical papillæ 0·3—0·5 of a millimeter in length, which project into the epithelium; but in children their presence is only indicated by slight inflections of the line of attachment of the epithelium.

The muscularis mucosæ, or muscular layer of the mucous membrane, consists of fasciculi of smooth muscular tissue running longitudinally, which are only feebly developed in the uppermost part of the œsophagus, where they are separated from one another by large quantities of the mucous tissue; lower down they become coarser and more closely approximated, so that the muscularis mucosæ here forms a continuous muscular layer.

The septa of the several fasciculi are continuous with the mucosa on the one hand and the submucous tissue on the other.

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* E. Klein, *Ueber die Vertheilung der Muskeln des Œsophagus*, etc., "On the arrangement of the Muscles of the Œsophagus;" *Sitzungsberichte der k. k. Akad. der Wissenschaften zu Wien.* Mai heft, 1868.

The thickness of this muscular layer is somewhat greater in general in the anterior wall of the œsophagus than in the posterior. The submucous tissue is about four times as thick as

Fig. 105.

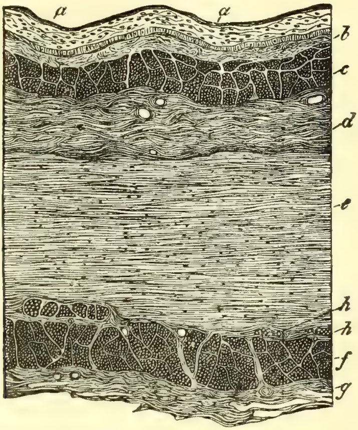

Fig. 105. Transverse section through the lower part of the œsophagus of the newly born Child. *a a*, epithelium; *b b*, mucosa; *c*, muscularis mucosæ; *d*, submucous tissue; *e*, layer of circular muscular fibres; *f*, longitudinal muscular layer; *g*, external fibrous layer; at *h h*, are seen two of the ganglia of Auerbach.

the mucosa, and is composed of longitudinal fasciculi of connective tissue fibres that run parallel to one another, and are always intermingled with finer and coarser elastic fibres. Vessels and nerves derived from the muscularis externa are found in this loose tissue, the nerves running obliquely towards the muscularis mucosæ. The fasciculi of the outer portion of the submucous tissue are directly continuous with the external fibrous membrane, and thus form the septa of the muscularis externa.

Acinous glands are rare and isolated, and less abundant in the posterior wall of the œsophagus than upon the anterior. On the latter they generally decrease in number from above to near the middle, but increase to some extent from this point downwards. They are small and oval, with their longer diameter arranged vertically; they lie in the submucous tissue,

close to the muscularis mucosæ, which their excretory ducts penetrate obliquely in a downward direction, opening on the surface of the epithelium with a constricted orifice.

The muscularis externa, or outer muscular coat, is composed in Man of an external longitudinal and an internal circular layer of fibres. The former is arranged in three divisions;* the middle, and by far the strongest, arising from a triangular elastic membrane attached to the posterior surface of the cricoid cartilage; the two lateral, which partly descend for a short distance internally to the circular layer of the œsophagus, arise from the elastic bundles in which a portion of the Thyreo-pharyngo-palatinus muscle terminates. The longitudinal fibrous layer in its further course is strengthened by the musculus broncho-œsophageus.† The circular fibrous layer gives off on each side the musculus crico-pharyngeus, and receives accessory fibres in the thoracic cavity from the musculus pleuro-œsophageus.‡ The circular layer continually increases in thickness as it descends, whilst the longitudinal layer, which exceeds the circular layer in thickness in the first fourth, continually diminishes as it descends.

The external muscular layer is not everywhere of equal thickness; in adults it is on the average 1·5 to 2 millimeters thick, and, according to Schmauser,§ is at the upper part more strongly developed on the anterior wall than upon the posterior,—then diminishes as it descends upon both surfaces, but especially upon the anterior, until in the lower third it is equally developed throughout the whole circumference of the tube.

A few smaller fasciculi, both from the internal circular and from the external longitudinal fibrous membrane are given off, which descend vertically, internal to the former, and external to the latter; the fasciculi are particularly large in the lower fourth, and are derived from the circular layer, becoming vertical as they descend.

The tendons of the fasciculi of the smooth muscular tissue

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* Henle, *Splanchnologie*, p. 141.

† Hyrtl, *Zeitschrift der Gesellschaft der Aerzte zu Wien*, 1844, p. 115; and Treitz, *Prager Vierteljahresschrift*, 1853, Band i.

‡ Hyrtl, *loc. cit.*

§ Schmauser, *Dissert. inauguratis*, 1866.

of the œsophagus extend, according to Treitz,* into the external fibrous membrane. The fibres of the muscularis externa of the upper fourth of the œsophagus in Man are for the most part transversely striated. But besides these, fasciculi of smooth muscular fibres are met with sometimes running vertically external to the longitudinal muscular layer, at others running circularly in the circular fibrous layer, and at others vertically between the fibres of this latter layer.

In the second fourth the smooth muscular fibres are so abundant that they sometimes exceed those of the transversely striated, predominating especially in the anterior wall amongst the longitudinal, and in the posterior wall amongst the circular layers of muscular tissue.

The muscularis externa, in its lower half, is composed of smooth fibres exclusively. Externally the muscular layers are invested by a fibrous sheath composed of connective tissue and elastic fibres, which for the most part run in a longitudinal direction.

At certain parts between the circular and longitudinal muscular fibre layers the nerves form quite a continuous layer, the branches of which perforate the circular muscular coat, in order to reach the submucous tissue. Amongst the nerves running between the circular and longitudinal layers ganglion cells, partly isolated, partly enclosed in a nucleated capsule, are found, as well as groups of ganglion cells united together by means of their processes; moreover, a few ganglion cells occur in the smaller nerve trunks as they run through the mucous membrane. Remak† has described true ganglia as being situated on the œsophageal branches of the vagus.

The lymphatics, according to Teichmann,‡ partly run in the mucosa, partly in the submucous tissue, but do not form a double capillary network as in the wider portions of the tube.

In the œsophagus of the *Dog* the muscularis mucosæ does not

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* Treitz, *loc. cit.*

† *Ueber peripherische Ganglien an den Nerven des menschlichen Nahrungsrohres*, "On the peripheric Ganglia situated upon the Nerves of the Alimentary Tube in Man;" Müller's *Archiv*, 1858, p. 189.

‡ Teichmann, *Das Saugader System*, "The Lymphatic System," *loc. cit.*

form a continuous layer, as in Man, but first makes its appearance in the middle of the upper fourth, in the form of isolated longitudinal fasciculi, which, in the lower half, surround at various points the acinous glands, and sparingly accompany their excretory ducts nearly to the epithelium. The glands throughout the whole length of the œsophagus form a continuous layer, the thickness of which considerably increases in its lower part.

In the loose submucous tissue, nodal points are scattered, consisting of stellate plexuses of elastic fibres which present a remarkable yellowish-green colour.

The outer muscular layer of the œsophagus in the Dog is arranged in a much more complex manner than in Man. It is only in the upper half of the first fourth that it is composed of an external longitudinal and of a stronger internal circular layer. In the lower half of the first and the upper half of the second fourth, both layers are equally well developed, and are composed of fibres decussating obliquely, and at right angles. In the lowest part of the second, and throughout the whole of the third fourth, the inner layer is thinner, and becomes longitudinal, whilst the external is thicker, and is now circular. In the upper half of the inferior fourth, three layers are constantly present: an internal longitudinal; a middle, which is the strongest, circular; and an internal, which is the thinnest, longitudinal. The latter is derived from the internal, but chiefly from the middle, which proceeded above from the external layer. In the lower half of the inferior fourth, three layers are constantly present: an internal oblique; a middle, which is the strongest, transverse; and an external, which is the weakest, longitudinal. The fasciculi of the outer muscular layer do not, therefore, pursue a rectilinear, but a well-marked spiral course.

Smooth muscular fibres first make their appearance at about the commencement of the lowermost fourth of the external muscular layer, but even there they are confined exclusively to the innermost portion, which, immediately above the cardia is composed of smooth muscular fibres alone. The remaining layers are composed of striated muscular fibres up to the point of entrance of the œsophagus into the stomach.

The nerves are arranged in the same manner as in Man, but they are more numerous. They lie between the internal longitudinal and middle circular layers, and present ganglion cells which are either scattered or are arranged in series one behind the other.

In the *Rabbit* the mucous membrane of the œsophagus resembles

that of Man, but its external muscular layer is like that of the Dog. The laminated pavement epithelium increases in thickness downwards. The mucous membrane is generally of looser texture than in Man. When a muscularis mucosæ exists, it is composed of an inner portion, which usually forms a delicate plexus, and a much thicker external portion containing longitudinal bundles of fibres, supporting, especially on its outer surface, large vascular trunks. The papillæ of the mucous membrane are few in number in the upper part, of unequal size, conical, with a broad base; but lower down they become more numerous, so that just below the middle they are in close proximity to each other.

The muscular layer of the mucous membrane is deficient at the commencement of the œsophagus; but at a somewhat lower plane it makes its appearance in the form of small scattered fasciculi, composed of a few unstriated fibres, running in a longitudinal direction, and separated by layers of mucous tissue of considerable thickness. In the lower fourth it forms a continuous layer about 0·04 of a millimeter in width, which is traversed by numerous vessels distributed to the papillæ.

I have not been able to demonstrate acinous glands in the œsophagus of the Rabbit. The external muscular layer, having an average thickness of 0·85 to 0·2 of a millimeter, is composed, like that of the Dog, of spiral fasciculi, which are thus arranged: In the uppermost portion there are two layers, nearly equal in thickness, of which the internal is circular, the external longitudinal in direction. In the second fourth the circular and longitudinal layers run more or less at right angles to their previous course, so that in the third fourth their relative position is entirely changed, and we now find an internal layer, consisting of longitudinal fasciculi, a middle of circular, and an external of longitudinal fasciculi. In the lowermost fourth, although the thickness of these layers differs, their disposition is unaltered. The most internal layer here becomes constantly thinner, whilst the middle and external progressively increase in thickness. The two first maintain the direction they possess above, but the greater number of the fasciculi of the external layer run obliquely. Unstriated muscular fibres first appear in the lower fourth, and in the external muscular layer of longitudinal fibres; at first, only in the form of small fasciculi, but lower down increasing so remarkably in number and size that they soon outnumber the striated fibres, both in the external longitudinal layer and in the external portion of the middle circular layer. In the lower parts of the inferior fourth the

smooth fibres do not merely replace the transversely striated, but occur in great numbers as a new formation, so that these external layers in the vicinity of the cardia exceed the two others in breadth.

Ravitsch* has found the following arrangement of the smooth muscular fibres to obtain in the Horse, Calf, Pig, Cat, and Rabbit.

In the *Horse* the muscular layers of the œsophagus are entirely composed of transversely striated fibres as far as the thickening that is found about 20—25 centimeters above the cardiac orifice; below the thickening, smooth fibres make their appearance in the inner layer, whilst they do not present themselves in the external layer till near the cardia.

In all the above-named animals the transversely striated elements extend in both layers of the œsophagus to a variable distance from the cardia, always ceasing sooner in the inner than in the outer layer. This last statement is, however, opposed to that which, as mentioned above, I have found to occur in the œsophagus of the Rabbit.

Ganglion cells are here still more frequently met with than in the Dog; not only scattered amongst the fibres of the nerves running in the external muscular layer, but also in the lower fourth, in the form of microscopic ganglia, situated between the middle and external muscular layers.

The mucous membrane of the œsophagus of the *Rat* is precisely similar to that of the Rabbit, in regard to all its parts—epithelium, papillæ, and mucosa—as well as in the distribution of the muscular layer of the mucosa. The external muscular layer generally divides into a stronger internal and circular, and a thinner external longitudinal layer. Here and there the external muscular layer exhibits in its lowest portions an internal, strongest, oblique; a middle, circular; and an external, thinnest, longitudinal layer. All the layers are free from smooth muscular fibres as far as the cardia.

The œsophagus of *Birds* presents many points of difference from that of Mammals. In the fowl the mucous membrane is from 0·5 to 0·8 of a millimeter thick, and is covered with laminated pavement epithelium, the uppermost cells of which are tabular, and separated from each other by a broad, remarkably sinuous, intervening substance; those

* J. Ravitsch, *Ueber das Vorkommen quergestreiften Muskelfasern im Œsophagus der Haussaügethiere*, "On the presence of transversely striated muscular fibres in the Œsophagus of domestic Animals;" Virchow's *Archiv*, Band xxvii., p. 413.

of the middle layers are polyhedral, but rather elongated; whilst those of the deepest layers are spheroidal, but usually somewhat flattened by mutual pressure, and when they surround a papilla, are directed obliquely towards its longitudinal axis.

The mucous layer succeeding to the epithelium is a thick felt-like structure, composed of decussating fibres of varying size. From the surface of the mucous layer numerous small, conical, vascular papillæ project into the epithelium. The glands of the œsophagus are tubular, and are situated in the mucous layer; they are limited externally by the muscular layer of the mucosa, and partially project through that layer with their extremities. The fundus of each exhibits from five to seven or more hemispherical projections, so that they resemble acinous glands. Their excretory ducts, as well as their pullulations, are bounded by a very thin membrana propria, lined by a delicate narrow columnar epithelium. In hardened preparations the cylinders are usually found empty (cup or goblet cells, Becherzellen), the flattened nucleus alone remaining attached to one side.

These glands are always isolated, increase in number towards the crop, and are more sparingly distributed and smaller as they recede from this towards the cervical and the thoracic portions of the œsophagus.

The muscular layer of the mucosa forms a continuous longitudinal layer of smooth fibres, situated external to the mucosa and its glands, and presenting, where it is in contact with the fundus of a gland, a slight projection and attenuation. Here and there small fasciculi are given off, which run for some distance circularly, and then again become longitudinal. The submucous tissue, containing the larger vascular trunks in its meshes, is continuous with the mucosa and the external fibrous layer of the œsophagus. The external muscular layer is exclusively composed of unstriated muscular fibres, grouped into larger or smaller fasciculi to form an internal circular, and an external, somewhat thinner, longitudinal layer. Between these two layers is an almost continuous nervous layer, in which are found numerous ganglion cells, either isolated or united into a plexus.

Towards the crop the mucous layer becomes more attenuated, and the glands fewer in number; but the circular muscular layer increases in thickness in relation to the longitudinal. In the crop itself the epithelium presents the same characters as in the œsophagus. The mucous layer is here thinner, and there are no glands.

The external muscular layer is more attenuated than in the œso-

phagus itself. The muscular layer of the mucosa is equal in thickness to that of the œsophagus, and is partially separable into an internal circular, and an external longitudinal layer.

Hasse* found no glands in the cervical portion of the œsophagus nor in the crop of pigeons, but in the thoracic portion flask-shaped glands appeared, with a long narrow neck, and an internal lining of tesselated epithelium. In incubating pigeons he observed a remarkable thickening at the sides of the crop, due to a growth of epithelial cells filled with oil-drops, and resembling those in the milk follicles of Mammals.

In the Newt and Frog the mucous membrane of the oral cavity behind the tongue passes directly into the mucous membrane of the intestinal tract, which has now become converted into a complete closed tube.

The œsophagus of the *Triton* consists of an epithelium, a mucous layer, an external muscular layer, and an investing fibrous membrane. The epithelium, like that of the oral cavity, is columnar. The several cells are conical, with the narrow end more or less prolonged; whilst the base, directed towards the free surface, is beset with long cilia. Their shape may either be simply conical or strongly ventricose near the surface, and then, becoming suddenly attenuated, send a long process into the deeper-lying parts; or they may exhibit, when examined in the fresh state, a nucleated swelling in this process. Between the penetrating processes of the superficial cells fusiform cells are interposed, and between these again are here and there spheroidal cells with relatively large nuclei. In transverse sections of the longitudinal folds of the mucous membrane the penetrating processes of the conical ciliated cells are not directed perpendicularly from the surface, but are curved at their extremities. Hence in many parts these processes appear to be continuous with the elements of the mucous membrane. The mucous membrane consists of broad fasciculi of connective tissue, which present a looser texture toward the external muscular layer, and there form larger meshes, whilst nearer the epithelium the tissue is more compact. Fasciculi of connective tissue penetrate perpendicularly to the surface between the fasciculi of the external muscular layer, decussating once or twice at their entrance into the mucous membrane, and thus forming numerous spaces

* C. Hasse, *Ueber den Œsophagus der Tauben*, etc., "On the Œsophagus of the Pigeon;" Henle and Pfeuffer's *Zeitschrift*, 3. Reihe, Band xxiii., p. 101.

of considerable size, which are either occupied by thin-walled large vessels, or, being lined with epithelium, probably belong to the lymphatic system. Amongst these fasciculi extending towards the surface are found a variable number of fusiform elements, with rod-like or elongated nuclei. These are directly continuous with the fusiform cells of the innermost fasciculi of the external muscular layer, and are consequently to be regarded as smooth muscular fibre cells.

There is consequently here no independent muscularis mucosæ. In the small and delicate meshes of the mucous layer, large, irregular, or spheroidal masses of protoplasm lie isolated from one another.

The external muscular layer consists exclusively of smooth muscular fibres, the contour of which is either rectilinear or sinuous, and which contain an elongated and often pointed nucleus. It is not everywhere of equal thickness, and does not throughout its whole circumference consist of two distinct layers; on the contrary, the external fasciculi interlace to a considerable extent with the internal, so that in transverse sections a close network of muscular fibres is found, interrupted only by a small quantity of connective tissue. In many instances the direction of the internal fasciculi is horizontal, and that of the external, oblique, or more rarely longitudinal.

There are no glands.

In the œsophagus of the Frog the mucous membrane is lined with ciliated epithelium, similar in thickness and form to that already described in the Triton. In preparations hardened in alcohol, nothing but cup- or goblet-shaped cells are to be found over tracts of considerable extent.

The mucous membrane is strongly developed; its fasciculi pursue a horizontal course parallel to one another from without inwards till they reach the epithelium, beneath which, becoming bent at right angles, they assume a plexiform arrangement. The portion in contact with the external muscular layer, that is to say, the submucous tissue, contains the larger vascular trunks in its meshes.

The acinous glands in the Frog form an almost continuous layer from 0·4 to 0·5 of a millimeter in thickness. The acini vary in size, and are rounded or oval in form. They are lined by an epithelium consisting of closely compressed, rounded, or flattened by mutual pressure, cubical, or cylindrical cells. No muscularis mucosæ exists in the upper part, but in the lower there is to be found in patches situated externally to the glands a not very strong layer of longitudinal smooth muscular fibres, from which, as well as from the circular layer of the external muscular coat of the upper part, a few fasciculi are given off, that penetrate between the glands.

The external muscular coat consists generally of an internal circular and an external longitudinal layer. Fasciculi of fibrous tissue of various size, given off from the fibrous sheath investing the muscular coat externally, penetrate between the muscular fasciculi, forming thin septa, and constituting the support of the larger vessels and nerves as well as of the capillaries and the smallest nervous twigs.

Before we pass to the consideration of the histology of the stomach we must investigate the mode of transition of the several layers of the œsophagus into those of the cardia. In the œsophagus of man the laminated pavement epithelium extends to the cardia, where it ceases with a dentated border, and is replaced by a columnar epithelium. The mucous layer in its more restricted sense becomes rapidly thicker, in consequence of the additional series of glands that here make their appearance; so that the muscular layer of the mucous membrane becomes constantly separated by a greater distance from the epithelium, and at the same time diminishes in thickness.

The submucous tissue in general diminishes in thickness at the cardia, and is divisible into an internal looser and an external more compact layer. In the former lie the great vessels, whilst the fasciculi of the latter penetrate between the fasciculi of the muscularis externa.

There are no acinous glands immediately above the cardia.

The external muscular layer shows the most important changes; the circular muscular fibres which are directly continuous with those of the cardia are most strongly developed just above it; at the cardia itself, and just below it, they again diminish in thickness. The disposition of the longitudinal fibres is similar, except that their fasciculi frequently decussate so that they form a dense plexus. At the same time, after assuming this plexiform arrangement, some of them extend into the circular muscular layer, surrounding its most external fasciculi in order to become still more internal at a lower point. According to Henle,* the longitudinal fibres of the œsophagus partly terminate at the cardia, but the majority are distributed upon the stomach, diverging from one another in various

* Henle, *Splanchnologie*, p. 161.

directions. The middle portion of the fibres of the right half of the œsophagus extends uninterruptedly in thick masses along the upper curvature of the stomach; the remainder radiate upon the anterior and posterior walls of the stomach in slightly diverging fasciculi, arranged in a plexiform manner towards the lower curvature, to which, however, they do not reach.

From the left half of the œsophagus only delicate fasciculi extend to the upper border of the fundus. Two sets of fasciculi attach themselves to the right and left diverging longitudinal fibres of the œsophagus, which, slightly curved outwards, and altering their course from the horizontal to the vertical direction, extend over the anterior and posterior surfaces of the stomach. These two sickle-shaped bands of fibres which decussate in their course downwards from the cardia upon the anterior and posterior wall of the stomach, are the continuations of the circular fibrous layer of the œsophagus.

The laminated pavement epithelium at the cardia of the DOG is replaced, as in man, by simple columnar epithelium; the mucous layer becomes thinner at the cardia, since the gland tubes there present gradually increase in size. Consequently the muscularis mucosæ, which in the lowermost portions of the œsophagus was situated between the glands for an area of 0·5 millimeter in breadth, becomes more externally placed in order to form a continuous layer at the base of the new series of tubes commencing at the cardia. The acinous glands of the mucous layer of the œsophagus do not cease at the cardia itself, but, becoming at the same time smaller, reach to a distance of three millimeters below the line at which the columnar epithelium of the stomach begins. These are sometimes, although rarely, only the lowermost lobules of a gland, the excretory duct of which opens directly at the boundary line between the œsophagus and stomach, so that above the upper wall at the inner end of the excretory duct the laminated pavement of the œsophagus ceases, whilst below the lower wall the columnar epithelium of the stomach commences. In other cases two rows of acinous glands are found at the commencement of the cardiac portion, the excretory ducts of which open between the tubes with narrow calibre, that here begin to be developed.

The submucous tissue of the œsophagus likewise diminishes in thickness as it passes through the cardia into the stomach. The external muscular layer undergoes the following changes at the same part:—

The fasciculi of smooth muscular tissue of the inner layer of the œsophagus lying next to the cardia, after having remarkably increased in size, and assumed a transverse direction, attach themselves, without any defined line of demarcation, to the circular muscular layer of the stomach, the fasciculi of which are likewise very strong. Those fasciculi of the inner layer that are more remote from the cardia, as they change their direction from the oblique into the longitudinal, enter the external longitudinal coat of the stomach, the innermost portion of which they form. They chiefly consist of smooth muscular fibres, and in order to reach the longitudinal muscular layer of the stomach, run outwards round the transverse fasciculi of the inner layer lying close to the cardia. The middle transverse layer of the lowest portion of the œsophagus ceases almost entirely after rapidly diminishing in thickness at the cardia, only a few transversely striated fibres, with the smaller part of the external longitudinal muscular coat of the œsophagus, passing into the external longitudinal muscular layer of the stomach, the most external portion of which they form. Amongst the transversely striated fibres which preponderate in this external layer are a few fasciculi of smooth muscular fibres. The middle and strongest portion of the external longitudinal muscular coat commences at the cardia itself, and is exclusively composed of unstriated muscle. This layer of smooth muscular fibres is consequently introduced between the fasciculi, chiefly composed of smooth muscles, which are derived from the more remotely situated portions of the internal layer of the œsophagus and the transversely striated muscular fibres proceeding from the external longitudinal muscular tunic.

Immediately after the passage of the œsophagus through the foramen œsophageum, isolated oblique and transversely striated muscular fasciculi are found in the external fibrous sheath. Whether these are derived from the longitudinal muscular layer of the œsophagus, or from the surrounding tissues, I am not at present in a position to determine.

In RABBITS the mucous membrane at the passage of the œsophagus into the cardia presents the same features as in man; but the external muscular coat differs in some respects both from that of man and that of the dog. For the internal longitudinal fasciculi, after diminishing in number and size, completely cease at the lower extremity of the œsophagus; whilst both the middle circular, and the external longitudinal layers, after they have become entirely composed of smooth muscular fibres, and are increased in thickness, pass each in nearly equal strength respectively into the circular and longitudinal layers of the cardia.

In the TRITON a few acinous glands occur just above the cardia, at the lower extremity of the œsophagus, in the form of a nearly circular zone, and exhibit the same structure as those in the œsophagus of the frog. They pass directly into the tubular peptic glands of the cardia, the excretory ducts becoming shorter, and their acini diminishing in number and size.

The smooth muscular fibres first appearing in the form of small fasciculi around the above-mentioned acinous glands, are arranged where the tubular glands are developed, as an independent muscularis mucosæ, situated externally to the tubes; whilst the fasciculi of the external muscular coat, which in the lower part of the œsophagus are not distinctly separable into two layers, are here grouped into an internal circular and an external longitudinal layer.

The same changes which occur in the œsophagus of the frog at the point of transition into the cardia are here in every respect repeated. The portion of the mucous membrane situated internally to the acinous glands, between them and the epithelium, diminishes in thickness in proportion to the reduced length of the excretory ducts of the glands. At the same time the glands decrease in size, are arranged in closer proximity to one another, and pass by gradual transition into the peptic glands, which are at first vesicular, but subsequently more elongated and tubular at their fundus.

The mucous layer consequently suffers a transposition, in a topographical point of view; for, whilst above it is situated between the epithelium and the glands, below it extends between the glands themselves, whilst it diminishes in thickness

from the lower end of the œsophagus towards the cardiac orifice.

Immediately above the cardia a muscularis mucosæ is still found external to the glands in the form of partly circular, partly longitudinal or decussating fasciculi of smooth muscular fibres, which, in proportion to the approximation of the glands to the surface, bend inwards in order that, since they always remain attached to the outer border of the glands, they may form a continuous muscularis mucosæ investing the fundus of the gland tubes at the cardia itself.

Where the acinous glands begin to undergo their modification, the submucous tissue of the œsophagus increases considerably in thickness, but again diminishes as soon as the tubular glands make their appearance in the mucous membrane. The external musculature augments in thickness towards the cardia, and is so arranged that, as in the dog, the layer of circular fibres at the upper part of the stomach to a certain extent constitutes a sphincter.

At the cardia numerous fasciculi from the external portion of the circular layer extend obliquely to the inner portion of the longitudinal layer, with which they become continuous after they have decussated with the fasciculi derived from the inner portion of the longitudinal layer, which are directed obliquely downwards into the external portion of the circular layer.

D. Stomach.

The mucous membrane of the stomach is in general easily moveable over the muscular layer, being connected with it by a very loose submucous tissue, and when the stomach is empty, or during the contraction of its muscles, it forms numerous transverse longitudinal folds of various size, meeting one another at oblique angles, and presenting a plexiform appearance. This is particularly well marked in the cardiac extremity and greater portion of the left side of the stomach; whilst in the region adjoining the pylorus, as is very distinctly visible in the rabbit, where the mucous membrane is more intimately connected with the muscular layers, the folds of the former are either altogether absent, or only sparingly present.

The epithelium is of the simple columnar variety, and, commencing at the border of the cardiac orifice in man, is equally distributed over the whole surface of the stomach. The individual cells form columnar or truncated cones, and in preparations that have been hardened in chromic acid are, over surfaces of considerable extent, cup or goblet-shaped.

The mucous layer of the stomach in the new-born child increases in thickness, though not quite regularly, from the cardia towards the pylorus; the tubular glands of the stomach are imbedded in it, in close proximity to one another, separated only by a sparing quantity of tissue. At the cardia the glands commence as short indentations of the mucous membrane; but, rapidly increasing in length, soon form cylindrical tubes opening separately, or by a single wider orifice common to two or even three. The fundus of the tubes is in most instances somewhat club-shaped, and more or less curved or contorted, and at the cardiac and pyloric portions it is divided into two or more smaller cylindrical branches. Commencing from the middle of the larger curvature, and proceeding towards the pylorus, the number of tubes in the fundus which do not present division at their extremities usually progressively predominates over those that are divided. At the pylorus itself, the nearer the point of its transition into the duodenum is approximated, the greater is the number of the tubes that assume the elongated simple form.

According to Bischoff,* glands of peculiar form are present in the region of the pylorus; according to Ecker,† the glands are generally only tubular, except those in the neighbourhood of the pylorus, which are acinous. Kölliker‡ found in a small zone of the cardia, and in the pale zone of the pylorus, compound tubular, but in the larger middle portion of the stomach, which becomes of a lively red colour during digestion, only simple tubular glands.

The columnar epithelium is continued into the gland tubes to a variable depth. The glands at the upper border of the cardia are lined throughout with this form of epithelium. At

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* Müller's *Archiv*, 1838, p. 513.

† *Zeitschrift für rationelle Medicin*, N. F., p. 243.

‡ *Gewebelehre*, pp. 400 and 402.

a distance of from one half to two millimeters below the upper boundary-line of the cardia, the columnar epithelium lining the tubes is replaced at the fundus of the glands by spheroidal or

Fig. 106.

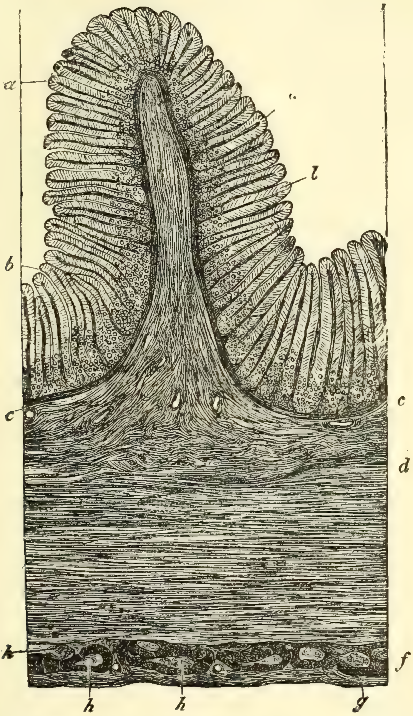

Fig. 106. Transverse section through the fundus of the stomach in a Child. *a a*, cylindrical epithelium ; *b b*, peptic tubes ; *c c*, muscularis mucosæ ; *d d*, submucous tissue ; *e*, circular muscular layer ; *f*, longitudinal muscular layer ; *g*, peritoneum ; *h*, ganglion of Auerbach.

elongated dark or pale strongly granular cells, often resembling bi-convex lenses. This replacement quickly extends upwards, so that the tubes soon appear to be lined with pepsine cells as far as their uppermost third. This relation obtains approximatively as far as to the middle of the large curvature. Commencing from the middle of the large curvature the columnar

epithelium reappears, extending farther down as the pylorus is approached, until at length it replaces the pepsine cells, even at the fundus of the tubes. In this respect there is, however, but little regularity, since tubes may be met with not far from the great curvature which are lined throughout with columnar epithelium; whilst, on the other hand, others occur near the pylorus, which, for more than half their extent, are lined by pepsine cells. We constantly meet at the pylorus with many (in some cases nearly all) of the gland tubes, both simple and compound, but especially the latter, that are lined throughout by columnar epithelium, in close proximity to others in which the sides, and in part the fundus, of the tubes are lined with pepsine cells, or next to those in which only the smaller part is covered with columnar epithelium.

In the newly born infant the columnar epithelium generally extends somewhat farther than half-way down the tube. After what has been stated above, it is impossible, therefore, to admit that there is any such distinction of two kinds of gland tubes, one lined by peptic cells, and the other with cylindrical epithelium as has been represented by Henle,* Kölliker,† Donders,‡ and Leydig.§ Gerlach,|| some time ago, noticed that, although the columnar epithelium extended to a greater distance down the tubes near the pylorus than at the fundus, still glands may even there be met with, the bottom of which is not covered with this form of epithelial cell. Mayer¶ and even Henle** have seen gland tubes in the pyloric region of the stomach of an executed criminal lined throughout with peptic cells. The wall of the glands found in the gastric mucous membrane is structureless. Henle†† observed in it, as well as in the membrana propria of other glands, small stellate cells, which, in preparations long macerated in chromate of potash, become smooth

* *Splanchnologie*, p. 157.

† *Würzburger Verhandlungen*, Band iv., p. 52.

‡ *Physiologie*, Band i., p. 204.

§ *Histologie*, p. 293.

|| *Gewebelehre*, p. 303.

¶ *Berichte der Freibürgen naturwiss. Gesellschaft*, No. 9, p. 147.

** *Loc. cit.*, p. 159.

†† *Loc. cit.*, p. 46.

and very finely granular. Henle also observed that the cells give off at the plane of the membrana propria from three to ten processes, which run in all directions, and which, whether broad or narrow at their origin, gradually become attenuated and branched, the branches communicating with each other. He therefore considered it probable that these cells are of a nervous nature, although he has in vain endeavoured to trace their connection with nerve fibres.

The tissue of the mucous layer is either a fibrous meshwork or adenoid tissue. The fasciculi of fine connective tissue occurring in and traversing the mucous layer in company with the vessels from the submucous tissue which penetrate the fasciculi of the muscularis mucosæ, unite frequently in a plexiform manner between the gland tubes, and include between their fibres a variable number of lymph corpuscles.

An adenoid network of cells, in the meshes of which lymph corpuscles are contained, is also found here and there between the extremities of adjoining gland tubes as well as just below the surface of the mucous membrane.

In newly born infants the muscularis mucosæ, or muscular layer of the mucous membrane, is from 0·01—0·05 of a millimeter thick, and in adults from 0·05—0·1 of a millimeter, and by its continuity separates the mucous from the submucous layer, forming consequently a level layer just external to the extremities of the gland tubes. The fasciculi of this muscular layer of the mucous membrane commencing from the cardia run chiefly in a longitudinal direction, but the internal fasciculi are partly circular and partly oblique, and the external longitudinal or oblique. Where the fasciculi of the one or the other layer run obliquely, they decussate; and if they were in the first instance internal and longitudinal, penetrate, after decussating, into the internal circular layer. They present an inverse relation, if before the decussation they constituted a portion of the internal circular layer; for in that case, after the decussation, they enter into the external longitudinal layers. Both from the internal and external longitudinal layers of the muscularis mucosæ small fasciculi are given off, which extend between the extremities of two tubes into the mucous membrane. Here they either run parallel, or, if they do not pass off at right

angles to the muscularis mucosæ, decussate with an adjoining fasciculus, in order then first to break up, forming a kind of pocket composed of smooth muscular fibres running perpendicularly to the surface and embracing the several tubes. The number of muscular fibres constantly diminishes towards the surface. When a few muscular fibres extend as far as the epithelium, they bend in a direction parallel to the surface, and are no longer capable of being followed in the sub-epithelial tissue, or they run between the fibres of fresh fasciculi, which here and there course in a direction parallel to the surface beneath the epithelium.

The submucous tissue which occupies the folds of the mucous membrane resembles that of the œsophagus, and just as the latter stands in relation with the septa of the muscularis externa, and of the external fibrous layer, so it is here in relation with the peritoneal investment, with the septa of the muscularis mucosæ, and with the mucous layer itself.

The thickness of the submucous tissue in the stomach of the newly born child amounts, in hardened preparations, upon the average, to 0·35 of a millimeter.

Lymph follicles, either in the form of glandulæ lenticulares, or aggregated into Peyer's patches, such as have been described as occurring in the stomach by Frerichs,* Bruch,† Bischoff,‡ and Kölliker,§ I have been unable to discover in any of the animals I have examined. It does indeed happen that certain portions of the mucous membrane of adults is more strongly infiltrated with corpuscles than others, but these spots have no definite limiting membrane. They may project to some extent from the surface, and may thus have given rise to the idea of their being proper lenticular glands.

In regard to the *lymphatics* of the stomach, we know from the investigations of Teichmann,‖ that in the dog they form a superficial plexus lying beneath the cæcal extremities of the tubular glands, and a deeper plexus situated between the muscularis mucosæ and the muscularis externa, and conse-

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* Frerichs, *loc. cit.*

† Bruch, *Zeitschrift für rationelle Medicin*, Band viii., p. 276.

‡ Bischoff, *loc. cit.*, Taf. xiv., fig. 4.

§ *Gewebelehre*, p. 403.

‖ Teichmann, *Das Saugader System*, etc., a. a. O.

quently in the submucous tissue. In the entire glandular bed no vessels of this kind are present. The vascular plexus above mentioned does not communicate with the capillary lymphatic system of the serous membrane directly, but through the intermediation of trunks provided with valves.

As Remak* has shown, and as has been corroborated by many histologists, the *nerves* of the stomach possess numerous ganglia, both in the muscularis externa and in the submucous tissue. I find in newly born children, that the greater number of ganglia are situated between the fasciculi of the longitudinal fibrous layer reaching externally to the peritoneal investment, and internally to the circular muscular layer, and forming, in parts, a continuous chain. In the submucous tissue, as in other parts of the intestinal canal, the nerves form a plexus, in which, as has already been mentioned, numerous ganglia are also found.

The external muscular layer presents, at the commencement of the large curvature of newly born children, a thickness of 0·95 to 1·1 of a millimeter; the circular muscular layer has a thickness of 0·7 to 0·85 of a millimeter. The fasciculi of this last do not here run parallel, but frequently decussate.

The fasciculi of the longitudinal muscular layer give off branching fasciculi, which, after frequent decussation, penetrate in an oblique direction into the circular layer. Smaller fasciculi also penetrate into the submucous tissue; these are continuous with the inner portion of the circular layer, and originate the fibræ obliquæ that will hereafter be described. According to Treitz,† they terminate in the mucous membrane with elastic tendons.

In the greater portion of the cardiac extremity of the stomach, a distinct division of the muscularis externa is to be observed, into an internal circular, and an external longitudinal layer, having a thickness of 0·25 of a millimeter.

In proportion as the pylorus is approximated along the greater curvature, the external muscular layer becomes stronger, which is effected chiefly by an increase in thickness of the circular layer, which amounts in the child to as much as

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* A. a. O.

† Treitz, *Prager Vierteljahresschrift*, etc., *loc. cit.*

1·144 of a millimeter. The fasciculi of the latter layer radiate obliquely, both towards the anterior and the posterior surfaces.

The fibræ obliquæ of the stomach, situated for the most part within the proper circular layer, have been accurately examined by Gillenskoeld,* according to whom the layer of oblique fibres is not so sharply defined from the circular as this is from the longitudinal, but the several oblique fibres are continuous with the circular, and each set passes into the other. The oblique fibres form a girdle around the cardia, and run on the anterior and posterior surfaces of the stomach, as far as the antrum pylori. In accordance with his description, two portions of the oblique layer may be distinguished; one superior and horizontal running in a forked manner over the left side of the cardia, and extending to the antrum pyloricum itself, whilst the other consists of shorter fasciculi, that run downwards, and sooner enter the circular layer. At the plyorus itself, when the stomach is continuous with the duodenum, the circular muscular layer in the infant attains a thickness of 2·64 millimeters, whilst the longitudinal layer is reduced to a minimum, the greater number of its fasciculi having entered the circular layer. The passage of the stomach into the duodenum is effected by this sphincter, which constitutes the valvula pylori. With the termination of the sphincter pylori, various changes occur; the gland tubes of the mucous layer become more simple, equal in diameter throughout, and completely lined with cylindrical epithelium. They are now called the Crypts of Lieberkühn.

In the submucous tissue, acinous glands occur in close contact with the muscularis mucosæ (Brunner's Glands), which, at first small, soon increase in size, and penetrate with their excretory ducts the muscularis mucosæ and the mucosa itself. Where the first lobuli of these glands occur, small fasciculi are given off from the external portion of the muscularis mucosæ, which run for a short distance external to the glands, and separate them from the adjoining submucous tissue.

Acinous glands consequently first make their appearance at the commencement of the duodenum.

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* Gillenskoeld, *Ueber die Fibræ Obliquæ in Magen*, "On the Oblique Fibres of the Stomach;" *Archiv für Anatomie und Physiologie*, 1862, Heft 2.

[In the DOG the tubular glands of the mucosa, like those of man, commence as short involutions of the mucous membrane lined throughout by a continuation of the columnar epithelium of the surface. At the commencement of the cardia they are divided and irregularly dilated at their extremity. About three millimeters lower down they assume the form of simple tubes, slightly dilated at their extremity. At the same time the columnar cells are replaced at the bottom of the tube by secreting cells, which gradually extend towards the opening; the glands coincidently becoming considerably increased in size. The ducts either open separately or several together.

From the middle of the larger curvature the pepsine cells are replaced again by columnar epithelium, in the same manner as in man.

The thickness of the mucous membrane also increases towards the pylorus in the dog as in man. On the inner surface of the longitudinal fasciculi of smooth muscular fibres proceeding from the œsophagus, and on the outer surface of the muscularis mucosæ at the cardia, where the tubular glands begin to be lined with pepsine cells, a layer of circular muscular fibres is superadded, at first feebly developed, but soon becoming thicker. The thickness of the muscularis mucosæ varies; in the fundus it amounts to 0·1—0·25 of a millimeter, and is here distinctly separated into an internal circular and an external longitudinal layer. In respect to their course and decussation, its fasciculi exhibit the same relations as in man.

The quantity of muscular fibres penetrating into the mucous layer between the glands is larger in the dog than in man.

The mucous membrane of the stomach of the RABBIT diminishes in thickness from the cardia towards the fundus, and from this point increases again towards the pylorus. The gland tubes it contains are similar in form to those in the stomach of the dog. In the fundus the individual tubes are a little wider than in the dog, and open by twos or threes into cylindrical fossæ, lined with columnar epithelium, which reach to one-fourth part of the thickness of the mucous membrane. The nearer the pylorus, the farther does the columnar epithelium extend down the tubes; moreover, this,

both on the surface and in the tubes themselves, in preparations hardened in chromic acid, is almost entirely composed of cup cells.

The muscularis mucosæ in the cardiac portion consists for the most part of longitudinal fasciculi, becoming somewhat stronger towards and in the fundus, and exhibiting here at most points a circular and longitudinal layer of equal thickness. In the pyloric portion of the stomach the fasciculi of both layers completely decussate with one another, and it is only at certain points that a distinct circular and longitudinal layer can be distinguished. Numerous fasciculi here branch off into the mucosa.

At the pylorus itself the muscularis mucosæ, and especially its longitudinal layer, increases five-fold in thickness. The submucous tissue, which is here, as usual, continuous with the septa of the external and internal muscular coat that dip into the mucosa in company with numerous vessels, is thinner in the pyloric region than at the fundus, and contains in its small meshes numerous spheroidal cells with a relatively large nucleus.

The external musculature consists exclusively, as in man, of smooth muscular fibres, and exhibits the following arrangement: The circular layer is particularly strongly developed at the cardia, but gradually diminishes towards the fundus. The most external fasciculi of the longitudinal muscular layer of the cardia are intimately connected with the fibres of the investing membrane, pursue an oblique direction, and farther down enter the circular muscular layer.

In the pyloric region the relations are altered, and the several layers have not only increased in thickness, but the innermost fasciculi of the circular layer become for a short distance oblique or longitudinal.

At the pylorus itself the muscularis externa presents the same arrangement as in the stomach of the dog,

The nerves and ganglia lying between the two layers of the muscularis externa form in parts a continuous layer, and in parts are sparingly distributed. Ganglia are not very frequently met with in the submucous tissue.

The stomach of the Rat presents remarkable peculiarities of

structure. Its left half may be regarded as a continuation of the œsophagus, whilst the right half forms the stomach in the proper sense of the word. The mucous membrane lining the latter portion is of a reddish-brown colour on the surface, like that of the fundus of the above-described animals. The two halves are divided by a fold which commences at the right extremity of the œsophagus that here enters the middle of the small curvature, and is so arranged as to open only into the left half; the communication of its orifice with the right half of the stomach being capable of entire occlusion by this arcuate fold.

The wall of the stomach is considerably thinner in the left half than in the right, at the cost both of the mucosa and of the muscularis externa. It is thinnest in the cæcal dilatation directed upwards, which the left half of the stomach forms at the junction of the large and small curvature. The left half of the stomach may also, from its structural characters, be regarded as a continuation of the œsophagus.

The laminated pavement epithelium increases in thickness from left to right to the summit of the fold, the height of which is about 1·5 millimeter, but again decreases on the right side, the uppermost cells first disappearing by becoming fused into a homogeneous layer; then the middle polyhedric cells vanish, whilst the deepest cells, which are arranged on the fold in the form of palisades and are cylindrical, increase in height, and commencing from the middle of the right side of the fold, cover the mucous membrane as a simple columnar epithelium.

The mucosa, which becomes stronger in passing towards the fold from the right, soon begins to form conical vascular papillæ, which are at first small, but with the increasing thickness of the pavement epithelium towards the summit of the fold increase in height.

The muscularis mucosæ exhibits the most important modifications. It is to it that the existence of the fold is essentially due. The nearer the fold is approximated, the more distinctly does it become differentiated into internal circular and the external longitudinal layers.

The former, rapidly increasing in thickness, ceases after attaining its greatest thickness at the summit of the fold, only the uppermost fasciculi remaining, which are now continued

into the circular layer of the muscularis mucosæ of the right half of the stomach. The external fasciculi of the longitudinal layer extend directly as such into the right half of the stomach; the internal fasciculi, however, decussate with the corresponding ones of the right half, and partly penetrate between the fasciculi of the circular layer.

The muscularis externa also increases considerably in thickness towards the fold, attaining its maximum at its base, and then gradually diminishing.

The tubular glands of the right half of the stomach are here also at first short, and lined by columnar epithelium, which, however, is soon replaced by rounded strongly granular pepsine cells, so that the columnar epithelium of the surface only penetrates as far as the upper fourth of the tubes.

The muscularis mucosæ of the right half of the stomach is thinner than that of the left, the fasciculi decussate to a considerable extent, but are here and there divisible into an internal circular and an external longitudinal layer.

The proportion of smooth muscular fibres which are given off into the mucous layer is here also considerable.

Numerous ganglia are situated on the nerves lying between the circular and longitudinal layers of the external muscular tissue.

In BIRDS the laminated pavement epithelium of the œsophagus ceases at the commencement of the glandular stomach with a dentated border, and is replaced by a simple layer of cylindrical cells.

The flask-shaped and, at their extremities, slightly lobulated glands of the mucous layer of the œsophagus, which have gradually augmented in number from above downwards, cease at the line where the columnar epithelium commences; and the muscularis mucosæ lying external to the mucosa, which diminishes in thickness where the œsophagus is continuous with the glandular stomach, becomes, in consequence of the disappearance of the loose submucous tissue, applied as a longitudinal muscular layer to the muscularis externa, so that it appears to form a single layer with this. In the lowermost portion of the œsophagus more or less sharply defined lymph follicles appear, which are either situated on the outer side of the glands, or externally between these nearly to the epithelium.

The surface of the mucous membrane exhibits a large number of capitate elevations, at the rounded apices of which the orifices of the gland sacs are perceptible. It further presents, in passing from above downwards, a continually increasing number of microscopic villi, minute folds or processes, which nevertheless are only the optical expression of the free terminations of the septa between two adjoining inflections of the mucous membrane, or rather of two adjoining short tubes, opening in immediate proximity with one another.

Bergmann* has described three types of glands: *a*. The well-known saccular glands, presenting a large central cavity, lined with cylindrical epithelium, which receives the orifices of all the smaller tubes lined with gland cells; *b*. A second type, found in the starling, sparrow, yellow-hammer, and crow, in strix flammea and colymbus, in which the several tubes open, by means of secondary ducts, into the principal excretory duct, which last may consequently be very short; lastly, *c*. He constructs a third type of those in which all the several tubes do not open by a common canal into the gastric cavity, but where a number of excretory ducts open in close proximity with one another, and the secretion of which is thus discharged into that cavity. (Cypselus apus.)

Between the extremities of the gland-sacs and the muscular layer a sparing quantity of loose submucous tissue intervenes, which, on the one hand, is continuous externally with the septa of the muscular fasciculi, and on the other supports the vessels, accompanied by which its cords penetrate between the several groups of glands, partly separating their walls, and partly extending into the mucosa. Amongst these fasciculi of connective tissue run, not only vessels which coil around and penetrate between the individual tubes, but also smooth muscular fibres.

In the inferior half of the glandular stomach the simple tubular glands increase in number and size towards the intermediate portion lying between this and the gizzard, in propor-

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† C. Bergmann, *Einiges über den Drüsenmagen der Vogel*, "A few Remarks on the Glandular Stomach of the Bird;" Reichert and Du Bois Reymond's *Archiv*, 1862, p. 581, fig. *c*.

tion as the gland-sacs diminish in size. The muscularis externa consists of three layers, because at the entrance of the œsophagus into the digestive stomach, the submucous tissue disappears. These are thicker at the point, corresponding to the space between the extremities of two adjoining saccular glands, than in those places where they are directly attached to their convex external portion. At the point of transition of the glandular stomach into the intermediate segment the fasciculi of the outer layers decrease in number and size, but those of the middle and internal layers augment, so that in the intermediate segment the external muscular tunic consists only of an external circular and an internal longitudinal layer.

In the mucous membrane of the *intermediate portion* of the fowl, straight, closely arranged tubular glands are met with, the extremities of which are somewhat narrower than their orifices, and are lined with spheroidal cells which gradually change as they pass upwards into the columnar epithelium of the surface. The tissue of the mucous membrane forms externally to the extremity of the tubes a thin, moderately dense layer, containing a variable quantity of lymph corpuscles, vessels, and nerves.

The muscular tunic consists of an internal longitudinal and an external circular layer; amongst the fasciculi of the latter are a few groups of fat cells.

In the intermediate portion the secretion of the glands becomes hardened into the form of a homogeneous thin layer covering the surface of the epithelium, through which homogeneous bands are prolonged in a vertical direction from the interior of the tubes. This layer investing the surface acquires a peculiar significance in the true muscular stomach or gizzard, where it forms a peculiar horny layer, at first thin, but gradually increasing in thickness as it descends, and when examined in thin sections with transmitted light, presents a deep yellow colour. The surface of the mucous membrane invested with this horny and, by reflected light, dark brown layer, forms at the commencement of the gizzard numerous tolerably regularly arranged corrugations, which however diminish in number and height, but increase in breadth downwards. The horny layer everywhere follows these elevations; with the in-

crease of the muscular layer, the horny layer also augments in thickness.

Leydig* originally stated that this layer is secreted by the gastric glands. It consists, in fact, of laminæ superimposed upon one another (consecutively hardened) which are interrupted at the points corresponding to the orifices of the gland tubes, so that these are continued through the horny layer in the form of a canal destitute of walls. It may be distinctly perceived in hardened preparations coloured with carmine that a homogeneous band proceeds as a direct continuation of the contents of the tube through the horny layer to the free surface. The columnar epithelium of the mucous membrane immediately subjacent to this layer is continued without interruption into the tubular glands. The several glands exhibit exactly the same structure as those of the intermediate portion.

I am unable, at least in the case of the yellow-hammer and fowl, to agree with the statements of Hasse,† according to whom two kinds of glands are present in the true stomach,—the simple and the compound tubular. The former, like the individual tubes proceeding from the gland-sacs of the crop, are partly lined with tessellated strongly granular cells, and partly with columnar epithelium.

As in the intermediate portion, there follows upon the glandular layer a close web of decussating fasciculi, constituting a muco-membranous tissue. The muscular layer, which at the commencement of this region is still very thin, becoming stronger as it descends by the development of numerous fasciculi, is also limited upon its outer surface, where it is still somewhat thin, by a horny layer in which numerous oblique striæ are perceptible that are continuous with the pointed muscular fasciculi that here take origin. Still more externally succeeds the investing membrane composed of oblique fibres which in some places is composed only of the tendinous expansion of the muscular fasciculi.

Both of the layers situated externally to the muscular layer

* Leydig, *Histologie*, p. 309.

† C. Hasse, *Beiträge zur Histologie des Vogelmagens*, "Essays on the Histology of the Stomach of the Bird;" *Zeitschrift für rationelle Medicin*, Band xxviii., p. 1, *et seq.*

diminish in proportion as that increases, so that where the muscular tissue attains its greatest thickness only a very few small striæ of connective tissue lie on its outer surface.

At the commencement of this region, as in the intermediate portion, the muscular tunic may be divided into two layers, an internal longitudinal, and an external circular layer.

In their further course the former, which constantly receives fresh accessions of oblique fibres from the mucous membrane, becomes first oblique and then circular. The external circular layer is likewise strengthened by numerous fasciculi, originally extending obliquely from without inwards, and arising from the horny layer limiting the muscular tunic externally. A considerable number of vessels and nerves run in the investing sheath of connective tissue.

After the remarks that have been already made respecting the passage of the œsophagus into the stomach of the FROG, little remains to be said in regard to the latter. The columnar epithelium of the surface, which, after treatment with chromic acid, is here likewise almost exclusively composed of well-defined cup cells, the individual cells of which exhibit at their attached extremity a longer or shorter cell process, continues without interruption into the closely approximated tubes of the mucosa. The cells lining the bottom of the tubes are spheroidal and finely granular.

The ciliated epithelium of the œsophagus does not entirely cease at the cardia, but is here and there prolonged for some distance; and even at a much lower level individual ciliated cells may occasionally be met with amongst the non-ciliated. The tubes, which are coiled or lobulated at their extremities, partly open by separate orifices, partly unite by twos in cylindrical pits which, as above mentioned, are lined by cylinder epithelium.

The muscularis mucosæ consists of an internal thinner circular and an external thicker longitudinal layer, the distinction between which is only clearly marked in the lower half of the stomach, whilst in the upper portion the fasciculi of the muscularis mucosæ are almost entirely longitudinal, or decussate to some extent with one another. Everywhere small fasciculi are given off, which penetrate between the tubes into the mucosa.

In the lower portions of the submucous tissue I find isolated, distinctly defined, usually oval lymph follicles, flattened from within outwards, in the capsule of which are contained numerous fusiform cells, with oblong, flattened nuclei. Some of the follicles are bounded by the muscularis mucosæ internally, and muscularis externa on their outer side, whilst others, as may occasionally be observed in the intestines of Mammals, penetrate the muscularis mucosæ, and extend to the cylindrical epithelium of the surface.

The submucous tissue itself, like that of the œsophagus, is moderately compact, and about 0·2 of a millimeter thick. The external muscular layer presents, though not uniformly an internal circular, and an external, much thinner, longitudinal layer.

In some places, instead of the latter, a few oblique fasciculi are found, which lower down enter the circular layer. Towards the pylorus both the circular, as well as the longitudinal layers which have here become independent, increase in thickness. The nerves and ganglia present the same relations as in the intestinal canal of the Vertebrata.]

E. SMALL INTESTINE.

By E. VERSON.

THE small intestine is a direct continuation of the stomach, and, like this, consists of an external peritoneal investment within which are two concentric tubes attached to one another by more or less dense connective tissue. The outer of these two is the muscular coat, the inner is the mucous membrane. The connective tissue forming the bond between them presents various degrees of thickness, but no peculiarities of structure; it contains a few elastic fibres and numerous connective tissue corpuscles.

The relative thickness of the two tubes to one another is too variable to admit of any precise statement being given; but in a general way it may be said that the muscular tunic is about three times as thick as the mucous, and that in Man the thickness of the entire intestinal wall, including the peritoneum, can scarcely be estimated at more than one millimeter. Measurements, however, taken at various parts, will naturally exhibit considerable variations according to the conditions of contraction or relaxation present in the muscular fibres.

The investing peritoneal coat is composed of ordinary connective tissue with elastic fibres, and is either directly applied to the muscular tunic, or is attached to it by means of a small quantity of loose connective tissue. Its free surface is covered by a single layer of pavement epithelium, the cells of which seen in profile appear as thin scales with projecting nuclei.

a. MUSCULAR COAT.

The muscular tunic of the small intestine is differentiated into two superimposed layers, which are distinguished in ac-

cordance with the direction of the fibres composing each, into an external longitudinal, and an internal circular. The former pursues the same direction as the intestine itself, the latter runs more or less at right angles to it, and embraces it with circular or spiral coils. A few fibres deviate from these two main directions, coursing round the muscular tube in a radial or oblique direction. Such fibres are occasionally found united into thick fasciculi in the upper portion of the duodenum, close to the pylorus, and they may be followed from thence, forming compressed spirals, into the longitudinal layer of the duodenum.

The muscular tube of the small intestine progressively diminishes in thickness towards the iliocæcal valve, the attenuation being particularly observable in the longitudinal layer, which in some of the lowermost parts may even be altogether deficient. The circular is generally thicker than the longitudinal layer, amounting in the adult to about 0·2 to 0·3 of a millimeter, whilst the longitudinal layer scarcely exceeds 0·1 of a millimeter in thickness. This proportion may, however, be reversed, strata of the longitudinal fibres being here and there found with corresponding diminution of the circular fibres.

The anterior surface of the duodenum is covered, as is well known, by a single layer of peritoneum, whilst the posterior surface is uncovered. At the lower curvature it is attached to the abdominal wall by an organic muscle, to which Treitz * has applied the name of Suspensorius duodeni. This consists of a few fasciculi of the longitudinal layer, terminating in tendinous fibres, that accompany the dense connective tissue surrounding the cæliac and mesenteric arteries, and are then lost. The fasciculi increase remarkably in breadth, and whilst they do not exceed two to three millimeters in thickness, are almost ten times that breadth. Additional fasciculi not unfrequently join them, derived from the diaphragm (right border of the foramen œsophageum and internal crua).

The duodenum has yet another muscular attachment at the head of the pancreas. In the duodenum of the child I find

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* *Ueber Einen neuen Muskel am Duodenum des Menschen,* "On a New Muscle of the Duodenum in Man." *Prager Vierteljahresschrift,* Band i.

the pancreas not in all instances sharply defined towards the longitudinal layer of muscles. This last frequently presents areas where acinous groups of the pancreatic follicles penetrate through foramina in it as far as the circular muscular layer, whilst at other points a few muscular fibres are given off from the longitudinal muscular tunic, which penetrate between the acini into the substance of the head of the pancreas. Even the circular layer may thus extend beyond its ordinary limits, and in longitudinal sections made close to the pylorus in the rat I have found a considerable fasciculus of smooth muscular fibres given off from it, which, like the fasciculi already described as entering the head of the pancreas, enter a group of Brunner's glands, and here similarly subdivide amongst the acini.

In its further course the muscular tube presents nothing remarkable, apart from its gradual attenuation, until it reaches the valvula coli. Throughout this, as is particularly observable in the new-born child, only the circular layer passes, whilst the longitudinal layer is interrupted; and indeed the bands of the latter, proceeding on the one hand from the ileum, and on the other from the colon, become considerably attenuated towards the free border of the valve, whilst many muscular fasciculi interlace with each other, and, finally, as my preparations show, arch towards the adjoining circular fibrous layer.

More or less considerable deviations from these arrrangements occur in different animals. Thus I may mention, that in the cat the longitudinal fibrous layer does not enter into the formation of the valve, but usually, like the peritoneum, extends uninterruptedly over it. On the other hand, the circular fibrous layer of the small intestine bears the relation to that of the large intestine, of a thinner tube (ileum), which is so introduced through a lateral aperture in the wall of a thicker tube (colon), that it projects with a free border into the lumen of the latter. In the dog, the circular fibrous layer of the small intestine projects in this manner with its free border, but this difference is observable, that the longitudinal fibres appear to be interrupted at the valve.

If a portion of the muscular tube, which can easily be detached with the forceps, be placed in a mixture of one part of

acetic acid and ninety-nine of distilled water, or in a solution containing 32·5 per cent. of liquor potassæ (Moleschott), it may easily, after the lapse of a few minutes, be broken up into fibre cells which, especially after the action of the acetic acid, exhibit a distinct nucleus, with one or two nucleoli. The muscle cells appear smooth, or sometimes angularly folded, and are seldom longer than 0·225 of a millimeter, and broader than 0·005 of a millimeter. No differences can be discerned in the size of the elements forming the longitudinal and circular fibrous layers respectively. In other Mammals, however, they may be both longer and broader, as is remarkably the case also in the Amphibia; those of the Proteus and Salamander being surpassingly large.

The several muscular fibres constituting the muscular tunic of the intestine are held together by a kind of cement. Their larger fasciculi are enclosed by bands of connective tissue, which divide the muscular substance when seen in cross section partly into numerous areas of equal size, and partly into larger segments, which embrace the whole thickness of the muscular tunic.

b. Mucous Membrane.

The mucous membrane constitutes the innermost tube, and exhibits peculiar elevations which project in the form of folds and villous processes into the lumen of the intestine.

The folds—termed also the valvulæ conniventes of Kerkringius—run more or less at right angles to the long axis of the intestine, and are either parallel to each other, or unite at acute angles, and always become separated by wider intervals towards the lower part of the small intestine.

The folds of Kerkringius are commonly regarded as persistent formations, because the muscular tunic does not enter into their interior. Nevertheless certain parts of the small intestine occur in children, where the muscular coat presents alternate contractions and relaxations. In the former these folds of the mucous membrane are sharply defined and prominent; whilst opposite the latter the membrane is perfectly smooth, thus affording strong evidence that the folds in ques-

tion are in some measure dependent upon the contraction of the muscular coat.

The villi of the small intestine, on the other hand, are elevations of the mucous membrane of more limited extent, which make their first appearance in the descending portion of the duodenum, where they are most closely arranged, and, becoming more and more widely separated from one another, extend

Fig. 107.

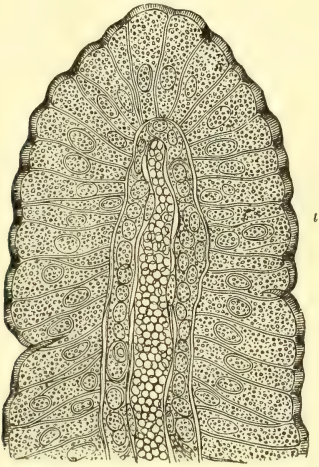

Fig. 107. Section of a villus. From the intestine of a Rabbit. *a*, epithelium; *b*, stroma; *c*, central cavity.

to the free border of the iliocæcal valve. They vary considerably in form. Sometimes they are cylindrical; at others conical or clavate, or flattened and expanded like a leaf—variations that in part, at least, are occasioned by the degree of contraction of the general muscular tunic and of their own muscular fibres, to which cause also their variation in length is attributable. In man the length of the villi is from 0·4 to 0·6 of a millimeter, and the breadth from 0·06 to 0·12 of a millimeter.

In every villus one or two, or more rarely three, central spaces are found, constituting the origin of the lacteals. (See Chapter IX. on the Lymphatics.)

The finer structure of the parenchyma of the villi is precisely similar to that of the rest of the mucous membrane, being composed of the tissue termed adenoid tissue by His; that is, of a plexus of anastomosing corpuscles, in the meshes of which cells are contained. These characters are not, however, equally well marked in all classes of animals, and variations may even be observed to occur in one and the same species, in accordance with age, the retiform tissue presenting a more uniform trabecular structure, or forming a delicate plexus of fibres, at the points of decussation of which a nucleus or two only may be discovered, the number of cells contained in the meshes having coincidently undergone considerable diminution. A similar transformation of the adenoid tissue of the mucous membrane may also be observed at certain points immediately beneath the epithelium—a circumstance which has led to the admission of a separate basement membrane, situated between the epithelium and the mucous membrane. No such membrane, however, can either be isolated or shown to form a continuous layer.

LYMPH FOLLICLES.—At the free border of the jejunum and ileum roundish or elliptical areas occur, with, in the latter case, their long axes corresponding to that of the intestine, and having a length of 1·5 centimeters, and a breadth of 7·20 millimeters. Their surface is convex, projecting into the lumen of the tube, and has either a few villi scattered over it, or is altogether destitute of them. These are the Peyer's patches, which, when examined with low powers, or sometimes even with the naked eye, appear as a group of roundish, pyriform, or more flask-shaped corpuscles, the so-called follicles. These dip into the submucous tissue with their rounded extremities, whilst their thinner ends form projections on the free surface of the intestinal mucous membrane, and must consequently pierce the muscularis mucosæ, the fasciculi of which, in point of fact, separate to permit the passage of the follicles.

A single Peyer's patch may include twenty or more such follicles lying in close contiguity, and only separated from one another by thin prolongations of the submucous tissue. The inferior or deep surfaces of the follicles are somewhat flattened,

whilst towards their upper part, especially above the muscularis mucosæ, the lateral boundaries disappear.

When examined with the microscope, these bodies present a remarkable similarity in structure to the so-called medullary cords of the lymphatic glands, and have recently even been

Fig. 108.

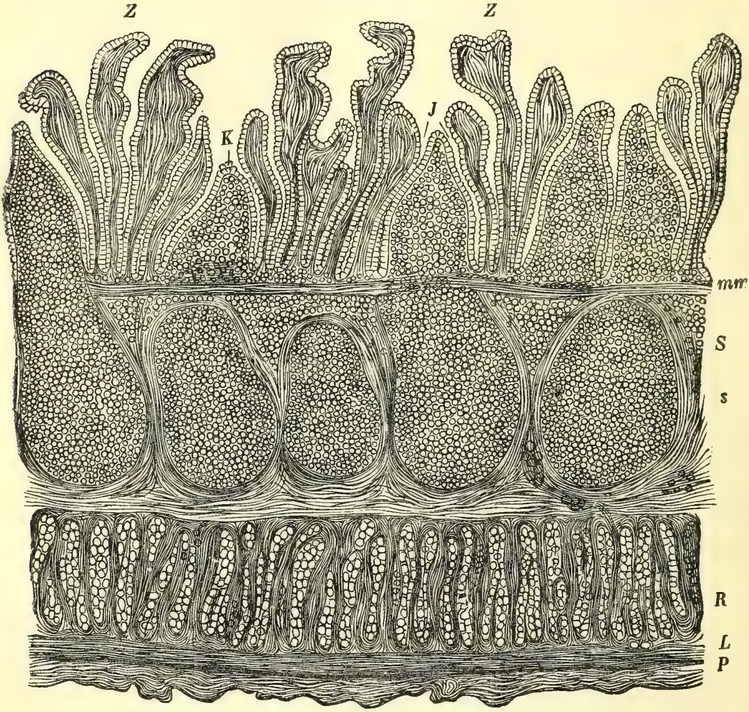

Fig. 108. Longitudinal section of the small intestine of a Rabbit. Z Z, villi; J, crypts; P, a Peyer's patch; K, cap of a follicle; S, submucosa; *m m*, muscularis mucosæ; R, circular muscular layer; L, longitudinal muscular layer; P, peritoneum.

regarded, in accordance with the views of Ziegler and Brücke, as really belonging to the system of lymphatic glands. However delicate a section may be that is made through a follicle, only an irregular accumulation of cells can be recognised; but if these be removed by pencilling with a camel-hair brush, or, still better,

by agitation of the preparation in a test-tube half filled with water, a network or plexus of fibres comes into view, similar to, though somewhat closer than that presented generally by the mucous membrane of the small intestine. The follicles consequently are composed of a plexus of fibres and of cells (lymph corpuscles) which fill the interspaces between them. But, just as the plexus of the mucous membrane presents histological differences under various circumstances, so may the framework of intestinal follicles differ, sometimes appearing as a tissue of anastomosing cells, the nuclei of which coincide with the thickened nodal points (child, rabbit), sometimes as a plexus of rigid hyaline trabeculæ (adult man, cat), and sometimes as a fibrous network (young dog).

The framework, whatever may be its form, is directly continuous laterally and above the muscularis mucosæ with the reticular tissue of the mucous membrane. In the deeper parts, on the other hand, the meshes gradually become more compact, and either, covered with epithelium, form the boundary of the so-called lymph sinuses, or, where these are deficient, are applied to the dense submucous tissue which constitutes the cord-like septa between the follicles, and extend to near the muscularis mucosæ. But in the event of the septa not reaching so high, the follicles just below the muscularis mucosæ may for a short distance be continuous with each other.

Regarded from another point of view, however, the framework is in direct connection with the vessels of the follicle, and, indeed, not only with the larger ones by means of their tunica adventitia, but also with the most delicate capillaries. This is effected by means of a fibrous network, and in well-prepared specimens the capillaries may be frequently observed to give off processes that suddenly become attenuated into fibres, which coalesce with those of the general mass.

As in man, so in the greater number of animals, the follicles reach the surface of the mucous membrane, and elevate this in the form of a cap (rabbit, sheep, calf, pig). It occurs, occasionally, however, that the follicles do not reach the surface of the mucous membrane, becoming continuous at some distance from it with the ordinary adenoid tissue of the membrane (cat).

Whilst the Peyer's patches constantly occupy the border of the intestine opposite the attachment of the mesentery, isolated or solitary follicles are distributed irregularly over its whole surface. These, like the Peyer's patches, are much more closely arranged in the lowest parts of the ileum. The number of Peyer's patches in the small intestine varies considerably. Authors calculate twenty to be about the average, though no definite limits can be given on either side. Where they are very numerous, they extend into the upper parts of the tube. Middeldorpf observed them even in the lower curvature of the duodenum.

GLANDS.—The secreting glands of the small intestine are constructed upon two different types, the acinous and the tubular, and are named after their discoverers, the former Brunner's glands, the latter, the Lieberkühnian follicles.

Brunner's glands agree exactly in their structure with that of other acinous glands of mucous membranes, and in man form groups of from five to ten acini, which open into a single excretory duct that traverses the mucous membrane, and opens on the surface. The diameter of the acini amounts to about 0·07 to 0·14 of a millimeter, and they consist of a structureless vesicle, the interior of which is lined with somewhat flattened cylindrical cells. The excretory duct is lined by similar epithelium.

The glands of Brunner lie imbedded in the submucous connective tissue, and form small masses, which may however attain sufficient size to cause the whole tunica nervea to disappear; and are bounded on the one side by the muscular tunic, and on the other by the muscularis mucosæ. The latter, however, forms no absolute limit, some of the acini being occasionally found projecting through it against the mucous layer, whilst, on the other hand, a few slender fasciculi of the muscle cells also accompany the connective tissue between the glandular vesicles, and then divide.

The greater portion of the glands of Brunner are found in the vicinity of the pylorus. In man, however, a few groups of these glands are distributed lower down the canal, whilst in other animals the whole series of glands form a single coherent

mass. The latter arrangement is remarkably well seen in the rat, in which animal the above-mentioned distribution of the muscular fibres between the gland vesicles can be easily demonstrated.

The *crypts of Lieberkühn* form tubular depressions of the mucous membrane, the blind extremities of which extend to

Fig. 109.

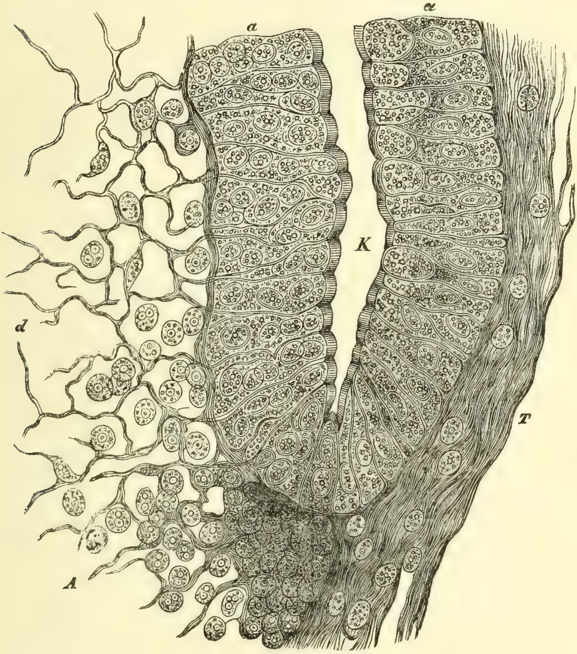

Fig. 109. Crypts and interfollicular connective tissue. From the intestine of the Rabbit. K, crypt; *a a*, epithelium; *d*, adenoid tissue, from which the cells have been removed by pencilling; T, fibrous tissue on the opposite side.

the muscularis mucosæ, and as they are arranged perpendicularly to the surface, they furnish a measure of the thickness of the mucous membrane itself. Their length varies from 0·34 to 0·5 of a millimeter, their diameter amounts to 0·06—0·08 of a

millimeter. The crypts are usually held to consist of a structureless membrana propria lined by a layer of cylindrical epithelial cells. The latter are identical with those forming the epithelium of the intestine generally, and the remarks that have been made respecting these apply to them also. The only slight difference that exists between them is, that the attached extremities of the cells forming the epithelium of the crypts are for the most part broader than the free extremities, which is intelligible when it is remembered that their free surfaces bound a tube of narrower diameter than the cryptic membrane itself.

In very fine sections of the intestine, from which the epithelium has been completely detached by delicate brushing, or where the epithelium is accidentally absent, it may easily be demonstrated that the so-called membrana propria of the crypts is not entirely structureless; for from the interfollicular trabecular tissue a few delicate fibrils penetrate into the basement membrane, and, preserving the longitudinal direction of the tube, run towards its orifice, near which they become continuous with a similar but transversely coursing fibrous tissue; this on the other hand, like the branches of a tree, is given off at almost right angles from the septal investing sheaths of the follicles. Such membranes moreover exhibit a beautiful rounded-polygonal pattern, corresponding to the bases of the detached epithelial cells.

The Lieberkühnian follicles occupy the whole free surface of the intestine, with the exception of the bases of the villi and the surface of the solitary glands. But whilst their orifices must necessarily be separated by the former, the tubes dilate beneath them in such a manner as almost again to come into contact, leaving only small interspaces for the passage of vessels and muscular fasciculi. They are usually altogether absent over the follicles, that is to say, of course, where these project into the lumen of the intestine, and here they are arranged like a coronet around the elevations, which has led to the employment of the term corona tubulorum by Johann Müller.

Muscularis Mucosæ.—Lying between the mucous mem-

brane and the submucous tissue, Middeldorpf * and Brücke † discovered a layer of organic muscular fibres, which can be traced from one end of the intestinal canal to the other, and from which processes are given off in various directions.

In the muscular layer of the mucous membrane two laminæ of nearly equal thickness may be distinguished, named, in accordance with the prevailing direction of their constituent fibres, the circular and the longitudinal fibre layer, though in some places they run into one another.

The muscular tunic frequently appears interrupted to permit the passage of the lymph follicles, and also to receive the cæcal extremities of the Lieberkühnian follicles; or, lastly, it may itself present a retiform arrangement, and it hence becomes intelligible how sections of the intestine sometimes exhibit continuous layers of circular and longitudinal fibres, sometimes only one of these, and sometimes neither.

We find, also, that in animals the prevalent arrangement approximates to one or other of these types, and I may mention that in the child the circular layer is subordinate, so that the direction of the fibres is almost entirely longitudinal, separating in some places to form beautiful plexuses, whilst in the rabbit the difference in the direction of the two layers is extremely well marked, though they are very thin.

We have already alluded to the processes given off by the muscularis mucosæ in speaking of the small fasciculi situated between the acini of Brunner's glands. Those, however, which pass towards the mucous membrane itself, and were discovered by Brücke ‡ and Kölliker,§ are of greater importance, and are more constantly present. These form, on the one hand, long bands, sometimes not exceeding a single fibre cell in thickness,

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* *De Glandulis Brunnerianis, Diss.* Vratisl., 1846.

† *Ueber ein in der Darmschleimhaut aufgefundenes Muskelsystem,* "On a muscular system discovered in the Intestinal mucous membrane;" *Akademie der Wissenschaften in Wien,* Februar heft, 1851.

‡ *Loc. cit.*

§ *Ueber das Vorkommen von Glatten Muskelfasern in Schleimhäuten,* "On the presence of smooth muscular fibres in mucous membranes;" *Zeitschrift für wissenschaftliche Zoologie,* Heft 1, 1851.

which run up between the Lieberkühnian glands, and, especially near the free surface of the mucous membrane are not unfrequently connected by a few transverse fibres; and, on the other hand, strong fasciculi, as many as twelve fibre cells in thickness, which penetrate the villi, and extend throughout their whole length. The muscular fasciculi in some instances enter the villi in the form of separate cords, but in others (especially in the smaller villi) first intercommunicate and diverge from one another at the bases, so that a double layer of muscular fasciculi may almost always be distinguished. One, lying close to the central lacteal, and helping with the epithelium to form its wall, the other running upwards in the parenchyma of the villi, traversing the meshes of the adenoid tissue, and frequently intercommunicating by anastomosing oblique fibre cells (His). The number of such fasciculi may amount to twenty or more in a single villus, as is well seen in the dog and cat, in which the longitudinal section of a villus often presents from seven to ten fasciculi in close proximity.

In the almost mature embryoes of guinea-pigs, instead of completely formed villi, we find solid papilliform masses of cells, with other similar structures presenting a central cavity extending for a variable distance towards the apex. In the latter a band of muscular fibres may be demonstrated, besides a few vascular loops, which, proceeding from the muscularis mucosæ, arch over the apex of the cæcal extremity of the cavity, and return again to the muscularis mucosæ. I have obtained a preparation exhibiting similar features, from an adult cat, and I believe that this affords an explanation of the statement made by Donders,* that transverse muscular fibres are present at the apices of the villi. I have myself not unfrequently seen them in the child, cat, and rat, and refer them to the above-mentioned loop running immediately beneath the free extremity. The fibre cells of the muscularis mucosæ are shorter and more slender than those of the muscular coat of the intestine, being, according to Moleschott, scarcely 0·06 of a millimeter long. The entire thickness of the muscular layer of the mucous membrane in man does not in general exceed 0·021

* *Physiologie*, Band i.

of a millimeter, but may amount to only one half of this, or even less.

EPITHELIUM.—The free surface of the mucous membrane is covered with columnar cells, usually arranged in a single layer, but presenting at some points,—as for instance over Peyer's patches,—rounded cells between their attached extremities.

The epithelial cells of the small intestine are sometimes columnar, sometimes conical, and in the latter case are attached by their apices, and present their bases to the cavity of the intestine. They undergo considerable modification from the action of reagents, becoming clavate, irregularly swollen, drawn out into long processes, etc.

The free border of the uninjured epithelial cells of the intestine presents a broad seam or hem, which under favourable circumstances (with good microscopes) exhibits a fine striation running parallel to the long axis of the cell. If the cells have already undergone change, the striæ become irregular, some of the lines projecting beyond the others—others ceasing to preserve their parallel arrangement. It has been a subject of discussion whether these striæ are the expression of fine canaliculi traversing the hem perpendicularly,* or whether they represent small rods of which it is composed.† This controversy has to a certain extent lost its importance, as neither the canaliculi nor the rods furnish any satisfactory explanation of the mode in which the absorption of fat molecules is effected.

Besides the ordinary columnar cells of the intestine, and constituting a very remarkable and frequent appearance, are cup, bell, or goblet-shaped structures, the open mouths of which are directed towards the cavity of the intestine, and which contain at their base a mass of protoplasm of variable size with or without a nucleus. Brettauer and Steinach‡ originally

* Funke, *Zeitschrift für wissenschaftliche Zoologie*, Band vi. Kölliker, *Würzburger Verhandlungen*, Band vi.

† Brettauer and Steinach, *Sitzungsberichte der Käiser. Akademie der Wissenschaften*, 1857.

‡ *Loc. cit.*

suggested that these structures were the results of the metamorphosis of the cylinder cells. It still remains doubtful, however, whether, as Henle* observes, these corpuscles are modified epithelial cells or represent morphological elements of a peculiar kind. The cylinder cells of the small intestine are structures of such delicacy that they can only be examined in the fresh state, without the addition of any reagents, and as they appear on folds of the mucous membrane excised from the living animal, the covering glass being very gently applied. It is only in preparations thus treated that the intestinal epithelium is displayed; it is only possible in this way to obtain a bird's-eye view of the regular mosaic formed by the cells investing the villi from their bases, and it is only thus that we can convince ourselves that both terminal surfaces resemble one another, varying only in their form and size. Even after the lapse of a few minutes, clear bright spots make their appearance at the bases of some of the villi, and in a short time goblet cells become visible. The adjustment of the focus renders it evident that these bright spots correspond to elevations which project at various points to an unequal height above or beyond the general level of the epithelium. Now, in regard to the occurrence of these elevations and the production of spheroidal structures from columnar epithelial cells, already demonstrated by Brücke from examination of cells in profile, there can be no doubt that portions of the contents of these cells are thrown off very quickly after their removal from the living body, and give rise to such cup-like structures. Stricker and Kocslakof have pointed out that a process of this kind is extremely well marked in acute catarrhal inflammation, the columnar epithelium of the catarrhally affected stomach and intestine of the rabbit, even in a fresh condition, presenting throughout tracts of considerable extent cup-shaped cells alone. If we add to this that it not unfrequently happens for the greater part of the intestinal epithelium to become converted, after the action of reagents into cup cells, we cannot in reason deny that the latter may originate from the ordinary columnar cells.

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* *Handbuch der Eingeweidelehre*, 1862, p. 165.

There is in all this, then, but little that is opposed to the view expressed by Leydig and F. E. Schulze, that the epithelial cells are to be regarded as one-celled glands; for we need only regard the material discharged by the cell as its secretion; and the cell wall, with the remainder of the contained material, as the gland. Further, it may be remarked that up to the present time there is no evidence against the supposition that it is only at a certain period of their development that the cells undergo metamorphosis into goblet cells.

Moreover, at present it cannot be denied that besides the epithelial cells from which the goblet cells already described originate, other peculiar goblet or tubiform structures are present. This has not indeed been absolutely demonstrated, but it constitutes no objection to the view that such structures cannot be seen in the fresh state, and cannot be distinguished from the artificial goblet cells under altered conditions.*

The cup-cell metamorphosis affects not only the cells, but as Basch† states, the nuclei; for when the intestinal epithelium of the frog is treated with boracic acid, similar appearances are frequently produced in them. The nuclei are then seen to be ruptured in one or two places, and masses of their contents not unfrequently project from the opening.

Heidenhain‡ maintained that the attached extremity of the cells of the epithelium of the villi, becoming gradually attenuated, is prolonged into a long process continuous with the connective tissue corpuscles of the parenchyma of the villi. These statements have been accepted, however, by only a few histologists, and have been denied by many.

Amongst the animals best adapted for the observation of the connection of the epithelium of the villi with a subjacent plexus, the guinea-pig may be named. In these animals and in the rat the epithelium of the villi frequently becomes de-

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* The now extensive literature of this subject is fully given in Eimer's Treatise *Zur Geschichte der Becherzellen*, "On the History of Goblet Cells." Berlin, 1868.

† *Centralblatt*, 1869.

‡ *Die Absorptionswege des Fettes*, "The Mode of Absorption of Fat;" Moleschott's *Untersuchungen*, Band iv.

tached from the parenchyma, like the fingers of a glove, and a delicate network then comes into view between the parenchyma and the epithelium, the threads of which are continuous now with the former, now with the latter. The appearances presented, however, are essentially due to manipulation. The network is composed of spheroidal cells, and the transition of such free but closely approximated cells into an apparent plexus may be distinctly followed.

Whether these spheroids are modified red blood corpuscles, or descendants of the epithelial or of some other cells, cannot be satisfactorily determined. Their appearance, and a comparison of them with red corpuscles altered by means of chromic acid, renders the former opinion the more probable one. In these animals then it is certain that no direct communication exists between the epithelium and the stroma.

It is more difficult to speak decisively on this point when the epithelium is not detached, since it is frequently requisite to decide whether two fibres lying in close proximity are continuous with each other.

NERVES.—Two thick layers of ganglionic nervous masses are distinguishable in the small intestine, one of which is situated in the tunica submucosa, and the other between the circular and longitudinal muscular fibre layers. The former, first described by Meissner,* is arranged in the form of a flat layer, although a few ganglia project towards the mucous membrane, and penetrate between the adjoining follicles; the latter, discovered by Auerbach,† is more irregular, presenting nodulated ganglionic masses, which are particularly large and numerous where the septa of connective tissue dip into the circular muscular layer.

The several ganglia may attain a diameter of 0·4 of a millimeter, and give off and are traversed by nerves varying from 0·002 to 0·004 of a millimeter in diameter, that form a plexus the branches of which penetrate the circular muscular coat with the septa of connective tissue, and establish a communication between the two ganglionic layers. Other branches pass

* *Zeitschrift für rationelle Medicin*, Band viii., 1857.

‡ *Ueber einen Plexus Myentericus.* Breslau, 1862.

through the longitudinal muscular layers, to join the mesenteric nerves. A few small scattered ganglia are distributed in the course of these nerves. In regard to the further distribution of the nerves in the mucous membrane, no certain information has been at present obtained, and the same may be said of the mode of termination of the pale nerve fibres in the organic fibre cells of the muscular tunics.

The nerve cells which, accumulated in numbers varying from three to thirty, form the ganglia, are in Man either unipolar or multipolar, and have a diameter of from 0·006 to 0·019 of a millimeter.

The nerves are composed of non-medullated fibres. Both the nerve trunks and the ganglia are invested by nucleated sheaths.

F. The Large Intestine.

The large intestine is the direct continuation of the small, and exhibits in its several divisions, the cæcum, with the processus vermicularis and the colon, the same structure and arrangement of its constituent parts as are presented by the latter. It is lined by a single layer of columnar epithelium, the individual cells of which not unfrequently vary considerably in size and shape; sometimes they are cylindrical or conical, with truncated apices, and are therefore short and relatively broad, and sometimes they are thin, and externally run into long processes; their nucleus is rounded or elliptical, and either occupies the centre or the lower, *i.e.* the external, third of the cell. In the newly born child the cylindrical epithelium may frequently be seen to be detached from the subjacent membrane. The thick hem or border of the columnar cells, both in fresh and hardened preparations, presents the well-known fine striation.

The *mucous layer* is similarly formed to that of the small intestine. It is composed of a very close, yet delicate plexus of cells, containing numerous lymph corpuscles in its meshes.

In the newly born child there are found, besides, numerous fusiform cells, similar to those met with elsewhere in embryonal connective tissue. The Lieberkühnian crypts are imbedded in the mucosa. They form sometimes straight, sometimes slightly curved tubes, arranged either perpendicularly or some-

what obliquely to the surface, generally of equal size throughout, or more frequently swollen at the extremity, and having a diameter of 0·06—0·08 of a millimeter, and a length of 0·35 of a millimeter. The epithelium lining each tube is a direct continuation of the columnar epithelium of the surface, and in no respect differs from it.

Fig. 110.

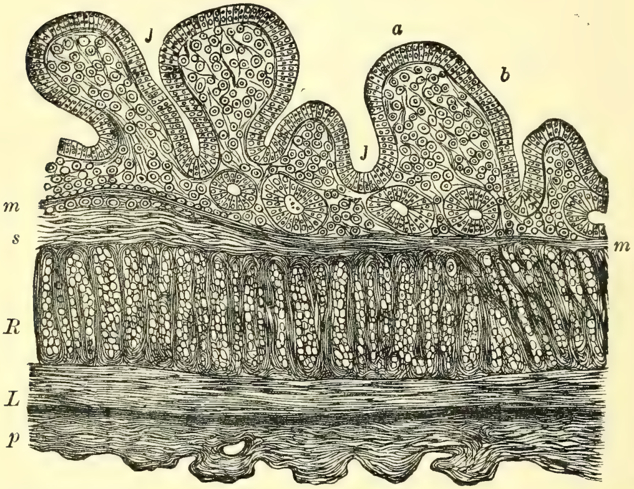

Fig. 110. Section of the large intestine of a Rabbit. J, crypts of Lieberkühn; *a*, epithelium; *b*, mucosa; *m*, muscularis mucosæ; *s*, submucosa; R, circular muscular layer; L, longitudinal muscular layer; *p*, peritoneum.

As regards the distribution of the crypts, they lie in close apposition in the cæcum and colon, whilst in the processus vermicularis they are generally separated from one another by wider tracts of mucous membrane, and at the same time appear shorter and broader.

The *muscularis mucosæ* is comparatively feebly developed; its fasciculi are partially arranged into one internal circular and an external longitudinal layer, which generally decussate at the base of the crypts, but frequently give off numerous smaller fasciculi that penetrate the mucosa between the tubes, to which they hold the same relation as in the small intestine.

The *submucous tissue* is looser in texture, and hence forms numerous folds or rugæ in the cæcum and colon, which are capable of being obliterated by extension. The submucous tissue stands here also in connection with the mucosa by means of the septa of the fasciculi of the muscularis externa, and also by the vessels which traverse the muscularis mucosæ.

The *muscularis externa,* like that of the small intestine, is arranged in two layers, an internal circular and an external longitudinal; the conjoint thickness of which in the cæcum and colon of the child amounts to 0·6—0·7 of a millimeter.

The thickness of the longitudinal layer is in inverse proportion to that of the circular; at the longitudinal bands they are both of equal thickness, but in receding from these the circular layer increases as the longitudinal diminishes.

The solitary follicles, as is generally admitted, possess no lacteals; but these, on the contrary, as Teichmann* has shown, are displaced by the follicles, so that their arrangement is much disturbed in their vicinity. The plexus surrounding the follicles consists, as shown by His, of wide lymph sinuses, which are lined by a flat epithelium.‡.

The *nerves* of the large intestine also present the same general relations as those of the small, both in regard to the plexuses they form between the two muscular layers, and to the ganglionic knots or swellings of Auerbach and of Meissner. The latter are usually spheroidal in form, of relatively large size, but containing singularly small cells.

The cells may be traced in the form of small chains for a short distance in the course of the several nerve trunks. Each nodal point is invested by a layer of connective tissue, in which, besides spheroidal nuclei, fusiform cells with oblong nuclei can be clearly distinguished.

G. RECTUM.

The thickness of the intestinal walls constantly augments as the anal orifice is approximated, so that near the middle of the

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* Teichmann, *loc. cit.* His, *Zeitschrift für wissenschaftliche Zoologie,* Bände xi., xii., and xiii.; Frey, Virchow's *Archiv,* Band xxxvi.

† v. Recklinghausen, *Die Lymphgefässe,* etc. Berlin, 1862.

rectum in the adult it attains a thickness of 3—4 millimeters The proportions are still more remarkable in the newly born child, in which the parietes of the rectum are from 1·3 to 1·5 millimeters thick. This thickening is partly independent and proper to itself, being in fact due to the increase of its own muscular layers, but is in part also attributable to extrinsic causes; the rectum, after leaving the peritoneum, receiving numerous muscular fasciculi from the adjoining parts, and in particular from the musculus levator ani.

The muscular tunics, of which the external here again forms a continuous layer, become in the lowermost parts constantly more and more closely connected with the adjacent tissues; and as the mucous membrane gradually passes into the external skin, the organic muscular tissue of the intestine blends with the transversely striated muscle in the neighbourhood of the anus.

The *peritoneum* also, where it invests the rectum, appears to be thickened, and the submucous tissue, which becomes steadily thicker and denser below, is partly continued directly into the subcutaneous connective tissue of the regio analis, and partly penetrates in the form of bands between the divisions of the musculus sphincter externus.

Muscular Tube.—The *longitudinal fibrous layer* of the intestine, which again forms a more continuous layer in the rectum, in consequence of the dilatation of the three ligamenta coli, still exhibits in the upper parts considerable differences in its thickness, suggestive of its previous fasciculated arrangement. In the newly born child, at this level, variations occur to such an extent, that in some parts the thickness amounts to 0·23 of a millimeter, whilst in others it does not exceed 0·06 of a millimeter; and similar differences occur in the adult. The muscular bands gradually become extended by lateral expansion, decussate in some parts with the outermost fasciculi of the circular muscular layer (at the valves of Houston), and finally become associated with the innermost fasciculi of the musculus levator ani, which, at first separated from them by a thin layer of connective tissue from the posterior portion of the pelvic fascia, ultimately join directly with them at acute

angles. A few millimeters higher a few fibres of the posterior portion of the longitudinal muscular layer mutually interpenetrate with those of the musculi recto-coccygei, which, proceeding from the sacrum, here terminate.

Three distinct portions of the musculus levator ani can be distinguished, each of which differs in the nature of its fibres from the other, the innermost being formed of organic, the middle of a mixture of organic and transversely striated, and the external (which constitutes the largest portion) of purely

Fig. 111.

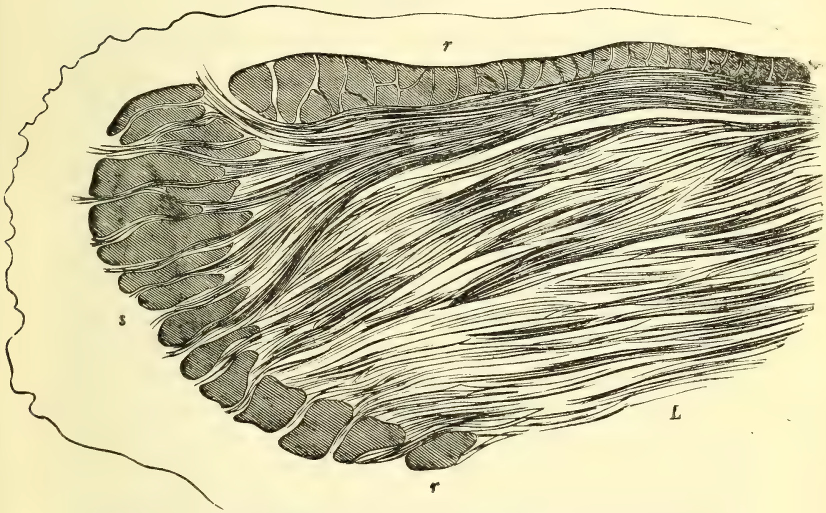

Fig. 111. Longitudinal section of the musculature of the rectum.

animal fibres. It is only the innermost of these three groups which enters into immediate relation with the rectum, its constituent fibres in part penetrating obliquely into the longitudinal muscular layers, and interweaving with them both in an upward and downward direction, and in part crossing them at right angles, and blending with the circular muscular layer. At the level of the sphincter internus the longitudinal fibrous layer becomes separated to some extent from the former, whilst fasciculi of connective tissue intervene between them; and the

limits between the longitudinal muscular layer and the innermost fasciculi of the levator ani, in consequence of their mutual approximation, can no longer be distinguished. The longitudinal muscular layer and the innermost fasciculi of the levator ani radiate out into numerous cords, which penetrate between the fasciculi of the musculus sphincter externus in such a way that the ring of the sphincter externus is split into a series of concentric zones; these traverse its whole thickness, and finally terminate in thin tendons, which are lost in the skin of the buttock.

The *circular muscular layer* at the beginning of the rectum still possesses a considerable thickness. In adults it measures somewhat less than one millimeter, and in the newly born child about 0·2 of a millimeter; but it increases in proportion as the anus is approximated; it forms also temporary thickenings in the lowermost plicæ sigmoideæ, where it interweaves with the longitudinal muscular layer, receives numerous muscular fasciculi from the levator ani, and finally near the anal orifice augments to a thickness of five millimeters in adults, and of 0·5 of a millimeter in the newly born child, causing an annular thickening termed the sphincter internus. The upper margin of this ring is by no means sharply defined, whilst if a longitudinal section be carried through the lowermost part of the rectum, the thickening caused by the sphincter internus is seen to be club-shaped.

Immediately below the sphincter internus, and situated somewhat more externally, the striated fibres of the sphincter externus begin to make their appearance, forming circles round the anal opening, and laterally blending with the most external fasciculi of the levator ani.

MUCOUS MEMBRANE.—The mucous membrane of the lower part of the rectum in man usually presents valve-like processes, running at right angles to the axis of the intestine, but usually extending over only a portion of the circumference. They are neither incapable of obliteration, nor invariably present, though the muscular tissue enters into their formation. In the great majority of cases I found them to be three or four in number, of which one, and indeed usually the lowest, appeared so far independent that a thickening of the circular

mucular layer corresponded to it, amounting to nearly double that which this layer ordinarily presents. In a specimen obtained from a child I found that in this way the circular muscular layer, which at first is 0·21 of a millimeter thick, becomes thickened opposite the fold to 0·4 of a millimeter, the longitudinal layer assisting in its formation by the incurvation of some of its fibres. The lowermost fold is situated about 5—6 centimeters above the anus (1—2 centimeters in the newly born child), and occupies the whole of the right wall of the rectum, and from thence may extend to some distance, both anteriorly and posteriorly. The one immediately above is situated on the left wall, and the next again on the right, and so on at short intervals, alternating from side to side when several valves are present.

The minute anatomy of the mucous membrane of the rectum presents the same features as those of other parts of the intestinal tract. Near the anus, however, the elastic fibres become more abundant, the cellular elements more sparingly distributed, the vessels less numerous, and ultimately it passes into the papillated external integument. The muscularis mucosæ may be distinctly followed to the point of transition. This layer also, like all the other tunics of the intestine, increases in thickness in the rectum, so that it may equal, or even exceed, 0·2 of a millimeter, whilst the differentiation of its fibres into an external longitudinal and an internal circular layer is lost in the prevailing longitudinal direction they assume. Near the anal orifice its fasciculi are closely arranged in the form of cords, which cause the projection of the mucous membrane into several longitudinal folds (Columnæ Morgagni), and then become continuous with delicate tendons which terminate in the skin adjoining the anus. The tendinous mode of termination of the muscularis mucosæ is much more easily recognisable in animals than in man, from whom it is difficult to procure sufficiently fresh specimens ; in cases where, as in the rat and guinea-pig, the line of transition from the columnar epithelium of the intestine into the tesselated epithelium of the skin occurs abruptly, it exactly coincides with this line.

The ascending processes which are here also given off by the muscularis mucosæ to the interspaces between the Lieber-

kühnian follicles are connected with each other by a few transverse fibres. These may be constantly seen around the orifices of the follicles immediately below the surface of the mucous membrane.

The *lymph follicles* of the mucous membrane of the Rectum are of the solitary variety, and comparatively few in number. In their general characters they resemble those of the other portions of the large intestine. It is deserving of notice, however, that in the child I met with isolated masses of adenoid tissue below the sigmoid curvature imbedded amongst the interweaving fibres of the circular layer, or lying between these and the longitudinal layer of muscular fibres, which were continuous laterally with the interfibrillar connective tissue of the muscular tunics. It remains to be established, however, whether these perform the same functions as the true lymph follicles.

At the thickened portion of the mucous membrane the *Lieberkühnian crypts* appear to be elongated, their length being as much as 0·6 and 0·7 of a millimeter, whilst they may attain to 0·07 of a millimeter in breadth. In the newly born child they have a height of about 0·3 of a millimeter and a breadth of about 0·05 of a millimeter. The only part of the surface on which they are not found is that over the lymph follicles, on which account the latter appear to be depressed, and can only be recognised with the naked eye as punctiform hollows. Elsewhere the crypts are situated in close apposition. They cease in the region of the Columnæ Morgagni, in the lowermost part of which a few sebaceous follicles already begin to be visible.

The *epithelium* of the large intestine, in conclusion, presents no points of difference from that lining the small, and like it possesses a striated hem or border. I have, at least, ascertained this to be the case in man, the dog, cat, rabbit, guinea-pig, rat, and frog. Near the anal orifice, however, numerous roundish cells constantly make their appearance between the columnar or conical ones, but this also occurs in many parts of the small intestine. The latter preponderate in number only as far as the Columnæ Morgagni, where they are gradually replaced by several layers of rounded succulent cells the most superficial of which become more and more flattened

till the transition into the ordinary tesselated epithelium is completed. In the child this transition is less sudden, because the projecting angles of the folds of Morgagni are already crowned with the pavement epithelium, though the more protected deep fissures between the columnæ always preserve an investment of cylindrical cells. Papillæ are first encountered where the pavement epithelium is completely developed—that is, immediately below the sphincter internus.

In the rat the Columnæ Morgagni are absent, and the lowest crypts extend to the sphincter externus. These lowermost crypts are lined throughout by the usual form of columnar epithelium, but on the side of these orifices which is turned towards the anus a layer of pavement epithelium, four or five cells in thickness, immediately abuts upon the cylinder cells, which last reach to the precise level of the orifice. This point coincides always with that at which the muscularis mucosæ, becoming oblique, runs out into points and is lost.

Nerves.—The plexuses both of Meissner and of Auerbach are continued from the colon into the rectum, the development of the latter preponderating over the former. After the peritoneal investment ceases, the close nervous web from the plexus pudendalis joins it, containing ganglionic enlargements of considerable magnitude. The above plexuses contain both dark-edged and pale sympathetic nerve fibres, which branch and are distributed between the muscular fasciculi of the sphincter internus and externus, and those of the external longitudinal muscular layer and levator ani.

CHAPTER XVII.

BLOODVESSELS OF THE ALIMENTARY CANAL.

By C. TOLDT.

Mucous Membrane of the Oral Cavity.

The mucous membrane of the mouth derives its supply of blood from various branches of the external carotid artery, the arteriæ labiales, buccinatoria, lingualis, transversa faciei pterygo-palatina, and alveolaris superior and inferior. The terminal branches of these arteries enter the submucous tissue of the oral cavity after the trunks from which they proceed have become much diminished in size from giving off numerous branches to the muscles, glands, and other organs, and after having formed numerous anastomoses with each other and the adjoining arterial vessels. After reaching the submucous tissue they are distributed parallel to the surface, and by their numerous anastomoses form a wide-meshed plexus, from which branches extend into the connective tissue layer of the mucous membrane, where they compose a close terminal network, interlacing with the corresponding venous plexus. From this finally the minute branches for the papillæ are given off, the capillaries of which present considerable variety in the different sections of the mucous membrane.

The efferent vessels of the papillæ discharge their blood into a close-meshed venous plexus, which decussates with the abovementioned arterial plexus. The venous portion of the vascular expansion contained in the connective tissue of the mucous membrane is characterised by the large size of the vessels composing it, their comparatively straight course, and numerous anastomoses, whilst the arterial portion is greatly inferior to the venous in the diameter of its constituent vessels,

which are at the same time somewhat less numerous. As a general rule the arterial and venous trunks pursue a parallel course.

The veins arising from the plexus each run by the side of an artery into the submucous tissue, where, having collected together and freely anastomosing with each other, they form a wide-meshed plexus similar to and parallel with that formed by the arteries. These relations are met with throughout the whole extent of the oral cavity, except only that the closeness of the plexus presents considerable variation at different parts, in accordance with the greater or less development of the capillaries of the papillæ.

As a general rule, it may be stated that the larger the papillæ, the more extensive is the capillary plexus in their interior.

At the *margins of the lips,* where the largest papillæ are found, from three to five branches of the terminal arterial plexus enter each papilla, and by their divisions and anasto-

Fig. 112.

Fig. 112. Papillæ of the lip.

moses form an elongated but wide-meshed capillary plexus (fig. 112). The transition into the venous channels takes place by one or more capillary loops usually situated at the apex of

the papillæ. From this point the small veins, characterised by their large lumen and straight course, receiving lateral branches, and occupying the axes of the papillæ, run towards the centre of their bases, and descend perpendicularly to the venous plexus of the mucous membrane. This course enables them to be easily distinguished from the capillary arterioles which run obliquely towards the papillæ. As we recede from the margin of the lips, the vascular arrangement of the papillæ assumes a more simple character, so that in those of the *posterior surface of the lips* the capillary loops are either simple, or have only one or two transverse branches. The papillæ of *the cheeks*, in like manner, have only simple capillary loops.

The papillæ of the *hard palate* are of considerable height anteriorly, yet, for the most part, contain only a single vertical vascular loop; posteriorly, the height of the loops is much diminished, and on the soft palate they form only flat arches, which, originating in the relatively close-meshed plexus of the mucous membrane, present the convexity of their arches to the surface.

The *gums* bear papillæ on their free surface, the vascular plexus of which is nearly as much developed as in those of the lips, but in those of the lateral surfaces there is only a single capillary loop.

The papillæ on the *floor of the mouth* have single loops, with occasionally one or two cross branches.

Langer * has very recently called attention to a remarkable arrangement that is found in the frog. In this animal the capillary vessels of the mucous membrane of the mouth and of the œsophagus as far as the cardiac orifice of the stomach present numerous diverticula, which project towards the free surface of the membrane, and, after becoming constricted, terminate in the capillary vessels. Langer is no doubt justified in regarding these as a peculiar arrangement supplying the place of capillary loops, and adduces, in support of his opinion, the fact that in the toad these diverticula are replaced by the ordinary

* *Sitzungsberichte der k. k. Akademie der Wissenschaften zu Wien*, Band lv., Abtheil 1; *Ueber das Lymphgefässystem des Frosches*, "On the Lymphatic System of the Frog."

capillary loops in the posterior parts of the mouth, and in the parts extending beyond to the entrance of the stomach.

Mucous Membrane of the Tongue.

The branches of the lingual artery, of which the dorsalis linguæ is distributed to the upper surface, and the arteria ranina to the middle and anterior portion of the tongue, run obliquely upwards and forwards into its substance, giving off numerous branches in their course, and ultimately, in order to reach the mucous membrane, penetrate the compact layer of connective tissue (fascia linguæ), which invests the muscular mass. On reaching the mucous membrane, these branches break up into a number of terminal twigs, which then pursue a superficial course, and finally form loops in the papillæ.

The simple filiform papillæ of the smallest size contain only

Fig. 113.

Fig. 113. Filiform papillæ of the tongue.

a single vascular loop; but all the compound varieties, whether filiform, fungiform, or circumvallate, possess a system of vessels from which a loop is given off to each secondary papilla. Into every papilla two or more terminal arterial branches enter (fig. 113), divide in the interior, and then, after anastomosing once or twice, give off a capillary branch into each

secondary papilla. The capillary has a diameter of about 0·01 millimeter, and runs to the apex of the papilla, where it forms a loop, and, reversing its course, unites with others to form a venous trunk. The large papillæ contain two or more venous trunks. The larger and smaller papillæ of the same variety, as well as the three subordinate forms of the papillæ, are not in any way distinguishable from one another by the arrangement of the bloodvessels, but essentially by the greater or less development of the vascular plexus, and the number of loops that are given off in each instance in correspondence with the number of the secondary papillæ.

The veins of the papillæ, which are of considerable size in the circumvallate variety, run vertically downwards, and form by their junction with those from other papillæ, and by their frequent anastomoses, a beautiful venous plexus situated between the terminal expansion of the arteries and the fascia linguæ. The meshes of this plexus are usually rounded in the anterior part of the tongue; the larger trunks arising from it penetrate the fascia, and, running side by side with the arteries, receive numerous veins from the muscles, and dip into the substance of the organ, where they coalesce to form the large venous trunks. In the posterior part of the tongue, numerous large veins take origin from the above-mentioned venous plexus, and, after running for some distance backwards on the fascia, combine at the root of the tongue to form the venæ dorsalis linguæ. The posterior parts of the mucous membrane of the tongue are consequently extraordinarily rich in veins.

It only remains to be mentioned that both the arterial and venous system of the mucous membrane of the right and left halves of the tongue are everywhere in direct communication at the median line.

Saccular Glands of the Mouth and Pharynx, and the Tonsils.

Arterial branches penetrate at various points through the fibrous sheath of the saccular glands into their interior, and give off branches which supply the adenoid substance. Where this last is distinctly divided into follicles, the capillaries are

distributed as in those of the intestine (to the description of which the reader is referred), except that their diameter is somewhat greater. But where the adenoid substance is diffused, the vascular plexus is quite irregular. The veins issuing from it are very numerous, and form short broad vessels, which for the most part run in the intermediate spaces of the adenoid substance, as well as immediately beneath the fibrous investment, from which they finally emerge a t various points.

Arterial branches also pass towards the mucous membrane, covering the sacculi internally, running up the interspaces between the follicles, or traversing the layers of adenoid substance, and finally terminating in flat capillary loops, which supply the papillæ. From these large venous trunks arise, which unite with those originally in the adenoid substance.

The bloodvessels in the several follicles of the tonsils exhibit the same relations; the larger arterial and venous trunks running and branching between them.

Acinous Glands of the Alimentary Canal.

All the various glands of the digestive tract present an essentially similar arrangement of their bloodvessels; as may be seen in the mucous glands of the mouth, pharynx, and œsophagus, the salivary glands and pancreas, and the glands of Brunner in the duodenum. The larger bloodvessels distributed to these glands ramify in the connective tissue investing the lobules. A single arteriole and veinlet penetrate each of the smallest follicles, then break up in a tree-like manner, and are finally lost in the capillary plexus. The capillary plexus everywhere consists of arched, frequently branched tubules; with a mean diameter of 0·008 of a millimeter, which are so arranged around the glandular vesicles that each of the latter is surrounded by from two to four such arches. These vessels communicate uninterruptedly throughout the entire lobule; each lobule thus possesses its own circumscribed capillary system. A round-meshed capillary plexus invests the excretory ducts of the mucous follicles as far as their orifice; the ducts are also accompanied by two veins which here and there communicate, and near the surface of the mucous membrane

usually join by means of an anastomotic ring with the venous plexuses of the mucous membrane.

Mucous Membrane of the Pharynx.

The upper parts of the pharynx receive their supply of blood through the pharyngo-palatine and spheno-palatine branches of the internal maxillary artery, whilst the middle and lower parts are supplied directly from the external carotid by the ascending pharyngeal and palatine arteries. The terminal branches of these vessels run obliquely towards the surface of the submucous layer, where they ramify, ultimately dividing into fine branches that run immediately beneath the epithelial layer of the mucous membrane. Capillaries, having a diameter of 0·006 of a millimeter, are given off from these vessels, which form simple loops in the serially arranged papillæ. There is scarcely any region where papillæ are found in which the vascular loops present so much uniformity as here. The descending portions of the loops unite into veins that quickly acquire a considerable size, and these vessels communicate by numerous anastomoses, and run for the most part in the direction of the long axis of the pharynx, so as to form a plexus with elongated meshes. Sooner or later the larger venous trunks join the veins of the subjacent glandular or muscular layer. The excretory ducts of the mucous glands are surrounded at their orifices with circularly arranged papillary loops.

Mucous Membrane of the Œsophagus.

The vascular plexus of the mucous membrane of the œsophagus, derived from the œsophageal arteries, and from small branches of the inferior thyroid and bronchial arteries, is extremely close. The larger vessels run longitudinally in the submucous layer, communicating from time to time by transverse anastomoses (fig. 114, *a*). The smaller branches reach the mucous membrane obliquely, and then usually become longitudinal and very sinuous in their course; they also form a plexus with elongated meshes (fig. 114, *b*), from which the capillary loops, destined for the most superficial layer, arise

fig. 114, *c*). In the upper part of the œsophagus these last are very similar to those of the pharynx, but are less uniform near the middle. Here the capillaries form flatter arches, with their convexities towards the surface, from which two to five short loop-like processes arise. In the lower parts of the œsophagus the simple loops are again found; they become

Fig. 114.

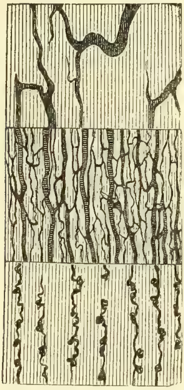

Fig. 114. Submucous and mucous layers of the œsophagus, as seen with different focussing.

more vertical, their height gradually increasing towards the stomach, so that near the cardiac orifice they attain a considerable size. At the point where the mucous membrane of the stomach commences they suddenly cease with a dentated border. The venous trunks of the superficial regions of the mucous membrane accompany the corresponding arteries throughout their whole course.

Muscular Coat of the Alimentary Canal.

The layers of smooth muscular tissue investing the alimentary canal from the œsophagus to the rectum, possess a vascular system proper and peculiar to themselves. The larger vessels reach them by two routes: on the one hand, branches are given off from the vessels supplying the intestine,

which penetrate the muscular tunic, and run for some distance between the longitudinal and transverse layers, to both of which their branches are distributed. On the other hand numerous vessels from the submucous plexus turn outward to the internal muscular layer, and penetrate the interspaces of its constituent elements. In the musculature of the stomach, which does not present quite such a regular arrangement, the larger bloodvessels nevertheless likewise run between the several layers and fasciculi.

The ultimate arterial and venous branches run transversely to the direction of the longitudinal muscular fibres, and give off numerous long capillaries at right angles, having a diameter of 0·007 of a millimeter; these, frequently branching dichotomously, run parallel to the muscular fasciculi, and communicate from time to time by short transverse branches. A very regular capillary system with elongated rectangular meshes is thus formed. If the muscles contract, the capillaries are thrown into curves, so that their characteristic appearance is essentially altered.

The vascular plexus of the muscularis mucosæ exhibits a similar arrangement; but, on account of the smaller thickness of the muscular layer, appears to have very large meshes.

Mucous Membrane of the Stomach.

The bloodvessels of the stomach enter it at the attachment of the peritoneal layers; each artery, accompanied by its corresponding vein, perforating the muscular tunic to reach the submucous tissue, in which they run for a variable distance, constantly giving off branches, or dividing dichotomously; the terminal branches of adjoining arterial trunks form frequent anastomoses. The smallest arteries traverse the muscularis mucosæ to reach the glandular layer, and divide into arcades of fine vessels, having an average diameter of 0·005 of a millimeter, which, winding spirally around the several gland-tubes (fig. 115), give origin to new arches, that do not, however, diminish in size. Every gland tube is thus surrounded by a system of capillary arches, which extends nearly to the surface of the membrane. At the same time it must

not be supposed that each follicle possesses its own independent capillary system; for, in point of fact, the capillary arches surrounding one freely communicate with those of the adjoining follicles. The rootlets of the veins commence near the orifices of the glands, in the form of thick arches, which run sinuously

Fig. 115.

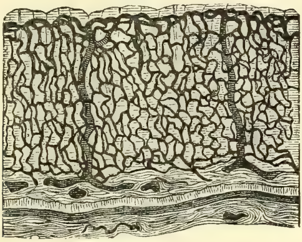

Fig. 115. Vessels of the walls of the stomach, as seen on transverse section.

towards the surface, and there unite to form smaller trunks. Several such trunks converge under the surface of the membrane to form a larger vein, which then descends vertically through the glandular layer. These vertical veins enter at

Fig. 116.

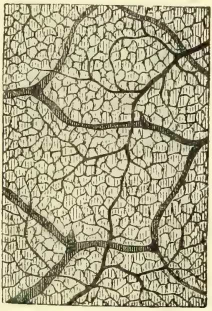

Fig. 116. Vascular plexus of the stomach, seen from the surface.

right angles into a wide polygonal-meshed venous plexus, which lies above the terminal expansion of the arteries, situated between the muscularis mucosæ and the glandular layer through the whole extent of the mucous membrane of the stomach.

Inasmuch as this plexus is exclusively composed of tubes of larger calibre, and is also exclusively fed by the above-described veins, it can be distinguished with remarkable facility when seen from the surface, as in fig. 116, from the arborescent terminal expansion of the arteries. From this venous plexus larger vessels take origin, which perforate the muscularis mucosæ, join the arteries, and, accompanied by them, traverse the submucous tissue, where they unite with others to form strong vessels that perforate the muscular tunic of the stomach.

Mucous Membrane of the Intestine.

With the exception of the large intestine, the arrangement of the bloodvessels of the mucous membrane throughout the whole extent of the alimentary canal is essentially similar, being modified only by the number and size of the villi, the distribution of the glandular follicles, Peyer's patches, etc. The arteries reaching the intestine between the layers of the mesentery perforate its muscular coat with the accompanying veins, and run in the submucous tissue chiefly at right angles to the axis of the tube. They communicate with each other by longitudinal and oblique branches, and form a wide-meshed plexus. The venous trunks accompanying them likewise form a plexus, which may be distinguished from that of the arteries by the more frequent anastomoses and the larger size of the vessels. If the intestine of the mature fœtus of the rabbit after injection be divided along the attachment of the mesentery, and the flat surface examined, this vascular network appears in the form of extremely delicate arcades, which, commencing at the attachment of the mesentery, extend on either side about one-third round the whole circumference of the intestine. Beyond this point the arteries and veins pursue a separate course.

The numerous branches proceeding from the submucous *arterial* expansion divide, after they have traversed the muscularis mucosæ, and have reached the glandular layer of the Lieberkühnian follicles, into capillary arches, which coil spirally around the glandular tubes, are about 0·007 of a millimeter broad, and extend to the surface of the mucous membrane, whence branches pass off to the villi. Other arterial

twigs ascend without branching between the gland tubes to supply the villi.

There are no proper *veins* formed from the capillaries surrounding the tubular glands, but the vessels collectively transmit blood into the capillaries of the villi. We must therefore regard the capillaries of the intestinal mucous membrane and of the villi as forming a common system, except that the latter receive special accessory arterial branches. The

Fig. 117.

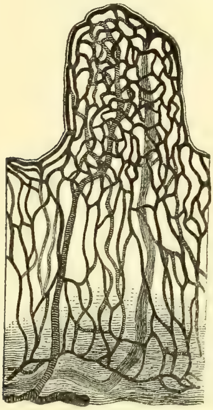

Fig. 117. Vascular plexus of the intestinal mucous membrane, seen in transverse section.

capillary system of the villi lies close to the surface, being separated from the epithelium by only a delicate homogeneous layer, and is tolerably close (fig. 117). It consists essentially of tubes, averaging 0·009 of a millimeter in diameter, which pursue a slightly tortuous course in the long axis of the villi, and communicate by numerous transverse tubules.

The arterial twigs above alluded to, arising directly from the vascular plexus of the mucous membrane, run singly or several in number to the villi, in which, after a short course, they break up into capillaries, and their terminal branches, after forming loops, may frequently be seen to enter the venous radicles. The relative numerical proportion of the longitudinal

and transverse capillary branches of the villi varies considerably in the intestines of different subjects, sometimes one and sometimes the other preponderating. The arrangement of the capillary plexus is also modified by the form of the villi. In those that have a flat conical shape, as in the duodenum, the transverse branches are usually smaller in number, whilst in cylindrical villi the longitudinally running vessels are less developed, and the transverse branches are consequently more numerous. In strongly contracted villi the capillary plexus appears closer, and the vessels more tortuous. The plexus is usually also more close near the apices of the villi. By the union of several arches of capillary vessels the venous radicles here originate, and, speedily coalescing, form a venous trunk of considerable size, which descends vertically through the villus, and joins with the veins of neighbouring villi.

In their further course the veins thus formed descend through the glandular layer without receiving any other branches or forming anastomoses, and finally terminate by entering the venous plexus lying subjacent to that layer. Where the villi are absent, as in the large intestine, the transition of the capillary plexus into the veins occurs in a precisely similar manner at the free margin of the folds which the mucous membrane forms around the opening of the tubular glands. The arrangement of the venous expansion beneath the Lieberkühnian glandular layer differs essentially from the arterial. Whilst the arteries break up in an arborescent manner into fine meandering branches, the veins are formed from the large venous trunks that descend from the villi. The venous plexus of the intestine is distinguished from the analogous one of the stomach by the more sharply defined limitation of the territory belonging to the several venous trunks, and by the more sparing occurrence of anastomoses.

In the large intestine the arrangement of the bloodvessels is similar to that of the stomach, with the exception that the capillary system surrounding the glandular layer is not so much ramified, so that in many parts only straight and but little branched tubules are found between the glands from which the close superficial venous plexus proceeds. The trunks collecting the blood from these extend downwards

through the glandular layer, and discharge themselves, like those of the stomach, into a wide-meshed plexus of large veins in the deepest layers of the mucous membrane.

Solitary Gland Follicles and Peyer's Patches.

These obtain their vascular supply from the submucous plexus of the intestine. The arterioles destined for *the follicles* proceed in part directly from the branches of the submucous plexus, and are partly branches of those trunks which break up into capillaries for the layer of tubular glands. The former chiefly run towards the base, the latter to the lateral surfaces of the follicles. The capillary system (fig. 118) consists of a

Fig. 118.

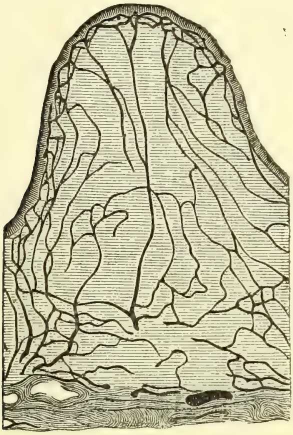

Fig. 118. Vascular plexus of an intestinal follicle, seen in vertical section.

plexus of vessels having a diameter of about 0·008 of a millimeter, with rounded polygonal meshes, which invests the whole surface of the follicle. From this plexus numerous fine capillary branches of 0·004—0·006 of a millimeter in diameter pass radially into the interior of the follicle. Near the centre they form communicating arches, not, however, with much regularity, since it frequently happens that three or more join to form one. Moreover, some few anastomosing

branches run directly across to the opposite side. It thus occurs that in the centre of the follicles a non-vascular space frequently remains, which, however, is not larger than such as may be found between the capillaries in the periphery. One or more of these communicating capillary branches also frequently extend straight through the middle of the follicle.*

The veins originate in the superficial plexus, especially from that situated at the base of the follicle, form short trunks which pursue a tortuous course, and partly coalesce with the veins of the villi, and partly open directly into a branch of the venous plexus lying upon the muscularis mucosæ.

The bloodvessels of *Peyer's patches* present a similar arrangement to those of the follicles. The plexus lying subjacent to them is characterised by its richness; the larger trunks, both arterial and venous, completely surround the margin of the groups of follicles, and send numerous branches beneath the follicles. The venous plexus is especially distinguished from that of the other parts of the intestinal mucous membrane by the circumstance that, besides the vertically descending veins of the villi, numerous smaller and larger branches proceeding from the follicles unite at more or less oblique angles to form larger trunks, and thus cause a considerable alteration in the otherwise characteristic appearance of this plexus.

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* For further information the reader is referred to F. Ernst, *Ueber die Anordnung der Blutgefässe in den Darmhäuten*, "On the Arrangement of the Vessels in the Walls of the Intestine." Zurich, 1851. His, in the *Zeitschrift für wissenschaftliche Zoologie*, Band xi., p. 416. Frey, in *idem*, Band xiii., p. 28.

END OF VOL. I.

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